Th. Scot.

"INDIGESTION".

A Study of some of the Nervous Mechanisms concerned in the production of Functional Disorders of the Stomach.

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INTRODUCTION.

Digestive derangement, in one form or another, is one of the commonest ailments that the general practitioner is called upon to treat. A very short experience of general practice is sufficient to demonstrate this; and the fact is soon apparent, also, that in only a small proportion of patients complaining of digestive troubles can actual organic disease be detected. In the vast majority of cases the trouble is of a minor nature, and not dependent on any actual organic change in the organs, but sufficient, nevertheless, to cause much real suffering and debility; and the problem of "indigestion" is a very real one. In many of these cases, examination of the stools may show no abnormality whatever. X-ray examination and test meals may reveal no striking departure in motility and secretion from the standard generally recognised as normal; and the "indigestion" in these cases does not stand for non-digestion, but for discomfort during the process of digestion. Furthermore, X-ray observations have shown that even in health there may be wide variations in the size and shape of the stomach, which the fractional test meal shows considerable variations in the composition of the gastric juice of apparently normal individuals. Similar variations occur in "indigestion". The patient complaining of greatest distress may be the possessor of a hypertonic, a hypotonic or a "normal" stomach; while in the matter of secretion he may show excessive secretion, "normal" secretion, or none at all. From clinical examination alone, therefore it is difficult to say exactly what is going on in the stomach, and what are the actual conditions of tone, etc., in the gastric wall.

Sir James Mackenzie (MACKENZIE[1]) says "Attempts are continually being made to classify affections of the stomach, and the lack of agreement in these classifications is merely due to the fact that attempts are made to differentiate what cannot be differentiated . . . To ascertain the true nature of many stomach affections it is necessary to wait and observe the results of treatment and the progress of the disease". This is at present, unfortunately, only too true. We must remember, also, that functional disorder of one part of the alimentary canal frequently depends on organic disease of some other part. Consequently, however convenient it may be for descriptive purposes to classify as complete diseases disorders of limited sections of the alimentary tract, we must always, in dealing with actual cases of disease, consider the tract as a whole. As Mackenzie points out, there is a great similarity in the symptoms of gastric diseases of the most varied kinds; most gastric symptoms are of a reflex nature, and capable of being produced by stimuli arising from the most varied causes, trivial or severe. Nevertheless it is reasonable to hope that increased knowledge of these reflexes and of the stimuli capable of calling them into action may yet enable us to differentiate many of the minor or functional derangements of the stomach, and so give us the clue to the correct method of treatment.

The importance of reflex phenomena in the case of the salivary glands was pointed out many years ago by Pavlov, who showed the variations that occur in the amount and the character of the salivary secretion with variations in the kind of stimuli presented to the buccal mucous membrane. Dry foods, for instance, such as meat powder or biscuit powder when introduced into the mouth of a dog with a salivary fistula, produced a much stronger flow of saliva than moist foods. Sprinkling an indifferent dry powder on the tongue excited one gland to activity and not another. Different chemical stimuli such as salts, bitters, acids, alkalies, gave characteristic responses from the different glands as regards the quality of saliva, the seat of action and the influence of local conditions on the results. These results depend on the discriminating ability of the peripheral end organs of the afferent nerves of the buccal mucous membrane in determining the nature of the material present in the mouth, and the amount and composition of the saliva best calculated to deal satisfactorily with it. Section of the nerves destroys the nicely calculated nature of the glandular response, and we must conclude with Pavlov that the sensory nerve endings in the buccal mucous membrane "officiate in deciding the most minute, exact, and highly specialised adaptation of the salivary glands to the nature of objects on which their secretions are poured out" (PAVLOV[2]). Pavlov showed, furthermore, that in dogs previously experimented on in this way, a response could be obtained from the glands by means of "psychic excitation". Thus in a dog with a salivary fistula, a flow of saliva is at once obtained on merely showing the animal a piece of meat. The saliva is of a viscid stringy nature, corresponding to that secreted when the animal is actually eating meat. If now the meat be removed, and pretence is made of introducing quartz pebbles into the mouth, no flow of saliva occurs (such pebbles do not stimulate the secretion of saliva, when actually introduced into the mouth). If, however, the pebbles are replaced by sand, and the dog (who has had previous experience of the introduction of fine sand into the mouth) imagines that the sand is to be again put in the mouth, a free secretion of thinner less stringy saliva is at once produced. Similarly, also, the sight of a bottle containing dilute acid (if associated in the mind of the animal with previous experiments), and the pretence of introducing such acid into the mouth, at once produces a free flow of saliva. This psychic excitation of course, can only occur in "educated" animals, and the reflexes involved have their starting point not in the end organs of the afferent nerves of the buccal mucous membrane, but in the end organs of eyes, nose and ears. Many factors enter into the production of the phenomenon, which depends, in part at least, for its successful accomplishment, on such incidental conditions as the surroundings of the animal, the presence of familiar attendants, the vessel containing the food or other material, etc. The results of the experiment therefore, are not so uniformly and unconditionally certain as in the case of direct stimulation of the buccal mucous membrane. The effect, in the case of the psychic stimulation, is dependent on a far greater number of conditions than in the physiologic, and the psychic reflex is therefore a conditional one, but "it never occurs without perceptible stimulation of some sense organ from without" (PAVLOV[3]).

These examples illustrate the importance of reflex processes as affecting the salivary glands. Similar, though perhaps less easily demonstrable reflex processes, play as important a part in the regulation of the activity of the gastric glands; and it is hoped that increased knowledge of such gastric reflexes will result in a clearer conception of the significance of some obscure gastric symptoms. In the study of the symptoms produced by disease of the stomach, or of any other organ, a consideration of the nervous control and the regulating processes is of fundamental importance, as it is by derangement of these processes that many symptoms are produced. The stomach, in common with other parts concerned in the digestion and assimilation of food, is under the control of the involuntary nervous system. Stimuli originating in the stomach may produce reflex symptoms in distant organs, the impulses travelling over the nerve tracts of this system; and conversely stimuli arising at a distance may, in like manner, produce end results in the stomach. Before passing to a study of disordered gastric function, therefore, it is necessary to examine not only the nerve supply of the stomach, but the connections and distribution of the involuntary nervous system as a whole.

THE INVOLUNTARY NERVOUS SYSTEM.

Our ideas as to the histology and physiology of that part of the nervous system which is not under the control of the will have been considerably modified, with advancing knowledge, during the past thirty years. Continental observers have contributed to the advances made, notably Koelliker, Dogiel, Van Gehuchten, Ramon y Cajal; but the main credit is due to Gaskell, Langley, and other workers of the English school. As Langdon Brown says - "To read an account of the sympathetic nervous system before Gaskell is like reading a description of the circulation before Harvey" (W. LANGDON BROWN[4]) "Just as even the course of the blood was in doubt till Harvey elucidated it, so even the direction of the impulses in the sympathetic chain was uncertain till Gaskell made it clear. But in both of these great works there are essential gaps. Harvey did not know of the existence of the capillaries, and Gaskell left many points still in doubt as to the course and distribution of the sympathetic impulses. Our gratitude to Gaskell must not blind us to our indebtedness to Langley, whose beautiful and accurate researches on this subject are of paramount importance. The elucidation of the plan of the sympathetic is due almost entirely to these two men."

The earlier anatomists were acquainted with the sympathetic nerve, which they regarded as arising from the cranial region, in the neighbourhood of the vagus. Its distinguishing feature, in their eyes, was the presence of knots or ganglia along its course. Haller first pointed out the presence of communicating nerves between the ganglia and the spinal nerves, and these he called "rami communicantes" (HALLER[5]). Following this discovery came the conception of a double nervous system, one, the central nervous system, controlling the organs of locomotion and sensibility, the other concerned with the regulation of the body nutrition. The discovery by Remak of non-medullated fibres belonging entirely to the sympathetic system (REMAK[6]), and the fact that the rami communicantes of Haller consisted partly of white and partly of grey fibres, strengthened the idea of two separate nervous systems, one with grey non-medullated fibres, the other with white medullated fibres, with, however, a reciprocal connection between the two, each system sending communicating fibres to the other.

Gaskell (GASKELL[7]), by cutting serial sections through the rami communicantes and the roots of the spinal segmental nerves after treatment with osmic acid, disproved the theory of reciprocal connection between the two systems, and showed that all the non-medullated sympathetic fibres were peripheral fibres; none of them actually entered the spinal cord. Onuchi's work, also, on the development of the sympathetic system, showed that the ganglionic cells arose from a group of cells which also gave origin to the posterior root ganglia. The cells in the sympathtetic ganglia, therefore, have a common origin with cells of the central nervous system, and have merely emigrated further afield than these latter. Gaskell, furthermore, showed that the nerve fibres which leave the spinal cord to enter the sympathetic chain were of a smaller calibre than the nerves to the skeletal muscles. He also discovered similar fibres in the cranial and sacral nerves, and demonstrated the relation between the white medullated fibres and the grey non-medullated sympathetic fibres. He concluded that the sympathetic cells consisted largely, if not entirely, of a system of motor cells situated on the path of efferent fibres from the cord to the peripheral organs."

Langley next devised the method of employing nicotine in the study of the sympathetic system. He showed that nicotine either paralysed the motor cells in the ganglion, or rendered the synapse impassable, so that stimulation of fibres passing from the spinal cord to the ganglion (ramus communicans) became ineffective, whereas stimuli applied to the grey fibre distal to the ganglion were still transmitted to the end structures. He applied the term "preganglionic" to the spinal fibres, and post-ganglionic to the grey sympathetic fibres. This method proved of great value in the study of the sympathetic, and he was able to show, in confirmation of Gaskell's work, that all "preganglionic" fibres (connector fibres of Gaskell) end in ganglia, and none go to the tissues direct. He also showed that all preganglionic fibres which innervate internal viscera pass through more than one ganglion (without interruption) before ending in the true motor cells of the sympathetic.

As already mentioned, Gaskell was the first to show that the connector fibres passing from the spinal cord to the sympathetic were of a much smaller calibre than the nerves to the voluntary muscles, and quite easily distinguishable from these latter in a cross section. He also found similar bundles of small fibres in the cranial and sacral nerves. These fibres subserve the functions of organic life, are not directly under the control of the will, and form collectively the involuntary or autonomic nervous system, which is usually sub-divided thus:-

1. Sympathetic system - thoracico lumbar outflow.
2. Parasympathetic system.
   (i) Cranial outflow:
      (a) From the midbrain.
      (b) From the Medulla.
   (ii) Sacral outflow.

The sympathetic nervous system arises from that part of the spinal cord included between the first thoracic and the third or fourth lumbar segments. Developmentally the neurones of the sympathetic system have wandered out from this part of the cord to supply the viscera, and they are still connected with this region of the cord by connector or pre-ganglionic fibres, whose cell bodies are situated in the lateral horn in a region extending from the first thoracic to the third or fourth lumbar segments. The sympathetic system includes (1) The GANGLIATED CORD of the sympathetic; a chain of ganglia lying on each side of the vertebral column, and prsenting usually one ganglion for each spinal nerve. The cords extend from the base of the skull to the coccyx. The cranial end of each is continued upwards through the carotid canal into the skull, and forms a plexus on the internal carotid artery: while the lower ends converge and end in a single ganglion (the ganglion impar) in front of the coccyx. Except in the cervical region, the number of ganglia corresponds closely to the number of vertebrae. The cervical region has three, the thoracic twelve, the lumbar four, and the sacral four to five. These ganglia are the lateral or vertebral ganglia.

(2) The COLLATERAL or PREVERTEBRAL ganglia, situated further away from the spinal canal; and TERMINAL ganglia, still more distant, situated actually on or in the muscles of the viscera.

(3) Numerous plexuses of fibres supplying the various tissues.

(4) White rami communicantes.

(5) Grey rami communicantes.

The white and grey rami communicantes establish communications between the sympathetic and the spinal nerves. The white rami are the connector fibres passing from the spinal segments to the sympathetic ganglia; while the grey rami consist of sympathetic fibres passing from the lateral sympathetic ganglia back to the spinal nerves to be distributed to the skeletal vessels, subdermal structures and the blood vessels of the spinal cord. Each spinal nerve receives a grey ramus communicans from the gangliated cord, but the white rami are supplied only, as Gaskell showed, from the first thoracic to the third or fourth lumbar nerves inclusive.

In certain areas, the ganglia of the gangliated cord fuse together. Thus in the cervical region we find only three - superior, medium, and inferior cervical ganglia - and sometimes only two - superior and inferior.

The sympathetic ganglia are masses of nerve cells and these cells and their processes form the motor neurones of the sympathetic system. The ganglia are highly important structures. They may be regarded as relay stations, where impulses are transmitted from one neurone to another, passing over the very important synapse in the process. Langley has shown that the fibres frequently pass through one or more ganglia without being interrupted in their course, or connecting with the neurones whose cell bodies lie in the ganglia concerned. All fibres which end in cells in a given sympathetic ganglion enter the ganglion as white, medullated fibres; while those which carry the impulse onward emerge from the ganglion as grey non-medullated fibres. All truly sympathetic fibres, therefore, are non-medullated. All medullated fibres belonging to the sympathetic system are purely connector in function, connecting the ganglionic motor cells with the cells in the lateral horn of the spinal cord.

Among the more important collateral ganglia are the ciliary, the coeliac (formed by the union of the semilunar and superior mesenteric), the inferior mesenteric, the renal and the ovarian or spermatic. Fibres from these ganglia form large plexuses before passing to innervate the viscera.

The SUPERIOR CERVICAL GANGLION is situated opposite the second and third cervical vertebrae. It receives fibres from the first, second and third dorsal segments of the cord. It innervates the vessels of the head, the muscles of the hair bulbs and sweat glands of the head, the musculus dilator pupillae and the smooth orbital muscle of Müller.

The MEDIUM CERVICAL GANGLION receives its fibres from the first, second, third, fourth and fifth dorsal segments. It communicates by its grey rami communicantes with the fifth and sixth and sometimes the fourth cervical nerves. It supplies fibres to the heart through the medium cardiac nerve, to the inferior thyreoid plexus, and to the common carotid plexus.

The INFERIOR CERVICAL GANGLION is probably formed by the coalescence of two ganglia which correspond to the last two cervical nerves. Through its grey rami it sends communicating branches to the seventh and eighth cervical and first thoracic nerves. It sends vascular fibres to the inferior thyreoid plexus, subclavian plexus, internal mammary plexus and vertebral plexus. It also sends fibres to the inferior cardiac nerve.

The STELLATE GANGLION is formed by fusion of the upper three or four thoracic ganglia. It provides visceral branches to the lungs, heart, aorta, oesophagus, and grey rami to supply the subdermal musculature and blood vessels of the anterior extremities.

The COELIAC GANGLION is formed by union of the semilunar, aorticorenal and superior mesenteric ganglia. It is connected with the cord by the greater and lesser splanchnic nerves, the former arising from the fifth to the ninth thoracic segments, and the latter from the ninth and tenth or tenth and eleventh. From the coeliac ganglion, grey sympathetic fibres pass to the stomach, liver, pancreas, spleen, kidney, suprarenal gland, ovary, testis, and the intestines as far as the descending colon.

The INFERIOR MESENTERIC GANGLION arises from the first, second and third lumbar segments. It sends grey non-medullated fibres to the descending colon, and through the hypogastric nerves to the rectum, bladder, sphincter of the bladder and genitals.

The WHITE RAMI COMMUNICANTES constitute the fibres of the connector neurones of the sympathetic system. They are the only efferent fibres connecting the cerebro-spinal system and the sympathetic, and they communicate to the motor cells of the sympathetic ganglia impulses brought from the central cells in those parts of the cord in which they originate. They spring from a group of small cells situated in the lateral horn of the thoracic and upper lumbar segments of the cord, emerge from the spinal nerves as medullated fibres, and remain medullated until they end in a motor cell in the sympathetic system. The impulse is then carried to its termination by the grey sympathetic fibre. Each medullated connector fibre is interrupted in this way, on its passage to the tissues it concerns, by one, and only one, synapse.

But in addition to these efferent connector fibres, the white rami contain medullated fibres whose nutrient centres are in the posterior root ganglia. "These are sympathetic sensory or afferent fibres. They carry impulses from the peripheral tissues supplied by the sympathetics to the central nervous system, where they are transmitted to the neurones and manifest themselves as visceral reflexes in the skeletal tissues. These are medullated throughout their entire course from the cells in the posterior root ganglia to the tissues in which they terminate" (POTTENGER[8]). The nutrient cells of the sensory neurones of the sympathetic system, then, are situated in the posterior root ganglia as in the case of the corresponding neurones of the voluntary system. The sensory fibres have no connection with the sympathetic ganglia, but pass direct from the tissues to the posterior root ganglia.

The GREY RAMI COMMUNICANTES pass from the vertebral sympathetic ganglia to <u>all</u> the spinal nerve roots. They run for a time with the spinal nerve and are then distributed to the smooth muscle which is supplied by the given spinal segment. In regions where several ganglia have fused e.g. in the cervical region, there is necessarily some degree of irregularity in the relationship between the grey rami and the corresponding spinal nerves.

The PARASYMPATHETIC SYSTEM. This includes the cranial outflow and the sacral outflow. Sections of the anterior roots of the second and third sacral nerves show, as Gaskell first observed, the presence of bundles of fine medullated fibres similar to those found in the thoracic and upper lumbar regions. These fine fibres unite to form the pelvic nerve, (nervus erigens) which differs from the white rami of the sympathetic in not entering a lateral ganglion. The fibres which compose it pass directly to ganglia lying on the surface of the large intestine, bladder and urogenital tract.

The CRANIO-BULBAR outflow of the parasympathetic system consists of bundles of fine medullated fibres found in the third, seventh, ninth and tenth cranial nerves. As in the case of the pelvic nerve, the fibres pass direct to the tissues supplied, and end in motor cells on or in the tissues in question. Fibres from the third nerve pass to the ciliary ganglion, and from there to the sphincter pupillae, musculus ciliaris and the m. levator palpebrae. Fibres from the seventh cranial nerve are found in the chorda tympani, which carries vasodilator and secretory fibres to the sublingual and submaxillary glands, to the mucous membrane of the nose and its accessory sinuses, soft palate and upper pharynx. From the ninth cranial nerve, vasodilator and secretory fibres pass to the parotid gland.

The most important part of the cranio bulbar outflow, however, is contained in the vagus, or tenth cranial nerve. This nerve emerges by eight or ten filaments, from the groove between the olivary and restiform bodies. It contains both motor and sensory fibres. The motor fibres arise from the cells of the nucleus ambiguus which may be regarded as corresponding to the ventral horn of the cord, from which the spinal nerves arise. There fibres pass to supply the voluntary muscles of the larynx, pharynx and oesophagus. A few of the sensory fibres of the vagus descend in the fasciculus solitarius and terminate round its cells. The visceral fibres originate in the nucleus dorsalis in the lower part of the floor of the fourth ventricle. From these origins the fibres pass through the ganglion of the root (ganglion jugulare) and the ganglion of the trunk (ganglion nodosum) and unite to form the vagus nerve. This passes down the neck in the carotid sheath, lying between the internal carotid artery and internal jugular vein as far as the level of the thyreoid cartilage, when the place of the internal carotid is taken by the common carotid. At the root of the neck the right vagus passes across the subclavian artery and passes by the side of the trachea to the back part of the root of the lung, where it forms the posterior pulmonary plexus. Two cords emerge from the lower aspect of this plexus and with branches from the left vagus, divide to form the oesophageal plexus. The lower parts of this unite again to form a single stem which enters the abdomen along the back of the oesophagus and is distributed to the posterior surface of the stomach, joining the left half of the solar plexus, and sending branches also to the splenic and coeliac plexuses. The left vagus enters the chest between the left carotid and subclavian arteries, crosses the arch of the aorta, and descends behind the root of the left lung to form the posterior pulmonary plexus. From here it passes to the anterior surface of the oesophagus forming, with its fellow, the oesophageal plexus, and is continued on to the anterior surface of the stomach, distributing branches to the fundus and the lesser curvature and some filaments to the gastrohepatic omentum and the hepatic plexus (GRAY[9]).

The sensory fibres of the vagus supply the following structures(POTTENGER[10]): the entire mucous membrane of the respiratory tract from the epiglottis downward: the heart: the base of the tongue, the palate, the pharynx and other portions of the mucous membrane of the throat, the oesophagus, stomach, duodenum, jejunum and ileum: the mucous membrane of the biliary passages: all musculature of viscera supplied by the vagus: that portion of the dura mater around the foramen jugulare: the concave surface of the auricula and the external auditory meatus.

The motor fibres supply the muscles of the soft palate: the constrictor muscles of the pharynx: the oesophagus: the stomach: the cricothyreoid, and in conjunction with the spinal accessory, all the other muscles of the larynx: the muscles of the bronchi: the muscle elements of the liver and spleen: the muscle elements of the suprarenal bodies and kidneys.

FUNCTIONS OF THE AUTONOMIC NERVOUS SYSTEM.

The autonomic nervous system comprises fibres concerned with the control of the functions of organic life. They are not under the control of the will, and normally do not convey afferent impulses which arrive at the level of consciousness. An individual in perfect health is not conscious of his internal organs, but the sense of well being associated with such a state may nevertheless be dependent on impressions conveyed to the brain from the viscera; impressions which do not pass the threshold of consciousness, but which affect and colour our individuality, and which become more clearly manifest in disease such as melancholia and hypochondriasis (LANGDON BROWN[11]).

The sympathetic and peripheral ganglia when examined histologically are found to consist of masses of nerve cells embedded in connective tissue, each cell being surrounded by a special sheath of endothelial cells. They differ from the cells in the posterior root ganglia in being multipolar: and each one probably possesses one axon and several dentrites, the latter ending in arborisations round adjacent cells. It was originally thought that these ganglia acted as centres for reflexes co-ordinating the activities of the viscera, and that they constituted in effect, an abdominal brain. This view, however, has had to be abandoned, and the ganglia must be regarded merely as distributing centres for impulses arising from the central nervous system. The essential part in a reflex arc, indeed, is not the nerve cell, but the nerve fibre; and the production of reflexes in a nerve centre depends on an interlacing network of such fibres with communications (synapses) between its constituent elements. The direction of the impulse and the nature of the corresponding reflex action varies with the strength of the original stimulus, the number of paths open to the impulse, and the degree of resistance met with at the different synapses encountered on the way. In the primitive nervous systems found in some invertebrates, the nerve cells lie outside the centres, and have one thick process passing into the nerve network, this process dividing later into axon and dendrites. Extirpation of the nerve cells, which can easily be carried out in these cases, does not abolish the power of the nerve net to subserve reflexes (STARLING[12]).

In the case of the sympathetic and peripheral ganglia, we have no such interlacing network of fibres; there are no connecting fibres between the different ganglia, nor between the different cells of a ganglion. All the fibres in a sympathetic ganglion have either entered it from a white ramus, or are destined to leave it in a grey ramus (STARLING[13]). Probably the pre-ganglionic fibre divides into several branches which arborise round the ganglion cells, whence new (grey) fibres proceed to carry the impulse to its termination. Thus we must regard the ganglia merely as distributing stations, allowing of a wider diffusion of the impulse coming from the central nervous system. This diffusion of the impulse was well brought out by Langley in the case of the pilomotor fibres in the cat. He showed that stimulation of a single grey ramus causes the erection of hairs over a single segmental area, whereas stimulation of a white ramus causes erection over a number of areas, usually five or six (LANGLEY[14]). The sympathetic nervous system is arranged, indeed, to produce generalised effects rather than localised accurate reflexes.

Although we must conclude that the sympathetic ganglia do not subserve true reflexes, nevertheless they are concerned in a group of phenomena closely resembling reflexes, but in which centripetal impulses are transmitted along centrifugal fibres.

These phenomena were first noted by Claude Bernard and Sokownin, but have been brought into prominence by Langley and Anderson, who have called them "pseudo reflexes" or "axon reflexes". They depend on the fact that the pre-ganglionic fibre branches before ending in a ganglionic cell, and the method of production is shown in the accompanying diagram (Fig. 1.) If all the nerves to the inferior mesenteric ganglion are divided, leaving only the hypogastric nerves, and then the left nerve is cut and its central end stimulated, we get a contraction in the right half of the bladder. Painting the inferior mesenteric ganglion with nicotine, which paralyses the plexus, prevents this effect, showing, therefore, that the ganglionic synapses are concerned in its production. Langley and Anderson, however, have proved that this is not a true reflex. If the nerve is cut at the point A. and time is allowed for degeneration to occur, stimulation at B. is ineffective. We must conclude, therefore, that we have been stimulating a pre-ganglionic fibre, and the results obtained were due to spreading of the impulse to other branches of this efferent fibre. Similar axon reflexes can be obtained along the abdominal chain on the pilomotor nerves, but in no case do they represent true reflexes.

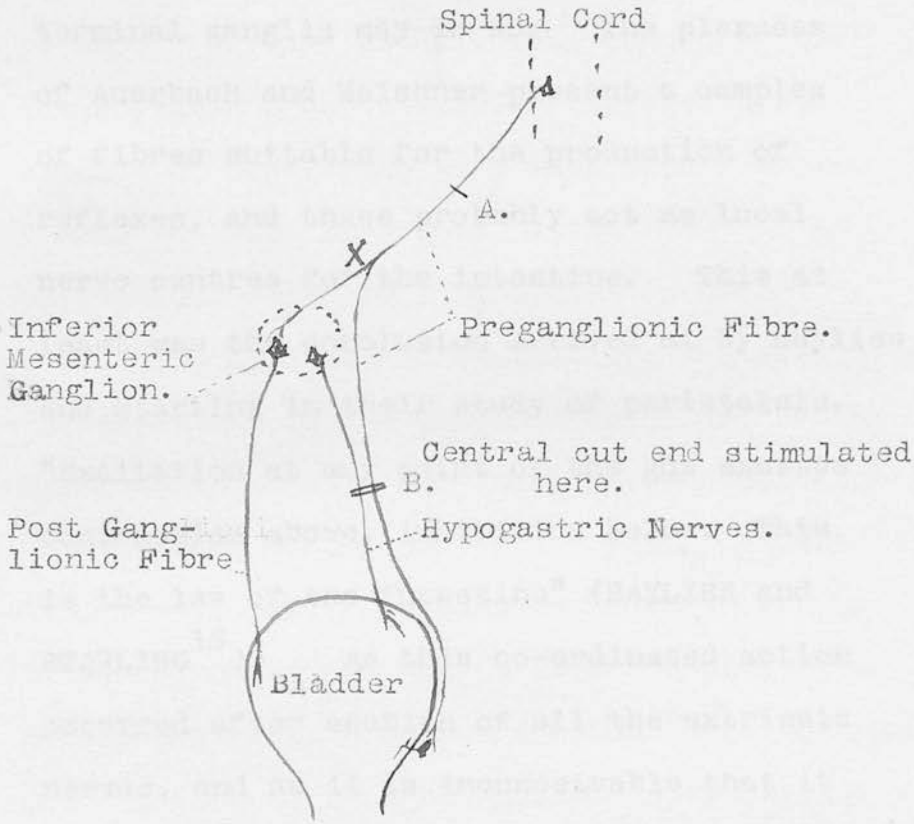


Fig. 1.

The production of an Axon reflex. The 'reflection' takes place at X.

STARLING E.H. Principles of Human Physiology. p.475.

Although the lateral and collateral ganglia then, probably do not act as centres for reflex action, it is possible that the terminal ganglia may do so. The plexuses of Auerbach and Meissner present a complex of fibres suitable for the production of reflexes, and these probably act as local nerve centres for the intestine. This at least was the conclusion arrived at by Bayliss and Starling in their study of peristalsis. "Excitation at any point of the gut excites contraction above, inhibition below. This is the law of the intestine" (BAYLISS and STARLING[15]). As this co-ordinated action occurred after section of all the extrinsic nerves, and as it is inconceivable that it should be performed by the muscles alone, they concluded that it was controlled by Auerbach's plexus. The injection of nicotine abolished true peristalsis - rhythmic contractions in a stretched ring of gut continued, but the waves of constriction which ran over the gut passed now as often in one direction as the other. Pinching the gut caused a local contraction which was not propagated, and a bolus placed in the intestine remained unmoved. These results were also obtained after painting the intestine with cocaine or injecting muscarine (Bayliss and Starling[16]) and the conclusion seems justified that they depend on the paralysis of the plexus. Bayliss and Starling concluded that the rhythmic contractions were myogenic and capable of travelling as a wave from fibre to fibre, but that they were unlike true peristalsis which is a co-ordinated reflex consisting of combined contraction and relaxation, and dependent on the proper functioning of the local nervous mechanism (BAYLISS and STARLING[17]).

A further function of Auerbach's plexus is probably that of making the muscle respond properly to stimuli coming from the underlying mucous membrane. Cannon (CANNON[18]) has pointed out that the peristaltic movements of the gut seem to be constantly modified by the chemical nature of its contents. Thus he observed energetic peristalsis after the injection of soapy enemata, and after the introduction into the lumen of the gut of a small cylinder of alkaline soap. Rushing peristalsis can be produced by cathartic drugs, which are irritants of vegetable origin, or salts only slightly absorbable, and the stimulus in these cases is apparently a chemical one, possibly affecting the neurones in Meissner's plexus and transferred thence to Auerbach's by means of connecting fibres (ALVAREZ[19]). In this connection also, Cannon points out that the different foodstuffs do not pass through the small intestine with equal speed, and yet when the end of the ileum is reached, practically all of the serviceable material has been absorbed: (CANNON[20]) a fact which seems to indicate some regulatory arrangement for the advancement of material through the small intestine, an arrangement probably dependent on the local nervous mechanism.

Still another function of the plexus is to act in opposition of the vagi and to prevent undue activity of the musculature (BAYLISS and STARLING[21]). Smooth muscle when cut off from its nervous connections is apt to undergo a great increase of tone, and the sympathetic has much to do with regulating the tone of the gastro intestinal muscles. The constant activity of the sympathetic in this direction is shown by the observation that when all the extrinsic nerves to the stomach are cut, gastric peristalsis and the rate at which the stomach empties approximate much more nearly to the normal than when the vagi alone are cut (CANNON[22]).

This antagonistic action of the sympathetic nerves and the vagus is but one illustration of the general law that when supplied to a common territory, the sympathetic and the parasympathetic oppose one another in their effects. Thus the sympathetic dilates the pupil, the parasympathetic contracts it: the sympathetic accelerates the heart, the parasympathetic slows it: the sympathetic diminishes the tone of the gastro-intestinal musculature and inhibits the movements of the digestive tract, while the parasympathetic increases the tone and stimulates the movements.

The results of stimulation of the sympathetic system are in the main katabolic, and as Cannon has pointed out, stimulation of the sympathetic accompanies conditions of excitement or great emotion, fear and rage: it is a defensive mechanism, called into play when the necessity arises for either fight or flight (CANNON[23]). As a result of splanchnic stimulation, the processes of digestion and assimilation are inhibited, sugar is poured into the blood from the liver, the splanchnic vessels contract and the blood pressure is raised, the distribution of the blood being rearranged at the same time, so as to give a more generous supply to the muscles, heart and brain: The heart-beats are quickened and made more forcible for the same purpose. The pupil dilates to give better vision and the secretion of sweat is increased in order to cool the body heated by the anticipated muscular exertion. Stimulation of the sympathetic, also is accompanied by stimulation of some of the ductless glands, particularly the suprarenals. The chromaffin cells of the suprarenals, indeed, have a common origin with the sympathetic cells, and this origin from the central nervous system accounts for the fact that their nerve supply consists of pre-ganglionic fibres. Gaskell has presented evidence that the sympathetic system, indeed, arose originally from nerve cells containing adrenalin, and this explains the remarkable fact that the effect of adrenalin on any part, is the same as stimulation of its sympathetic nerve. The sympathetic system has been evolved for the production of rapid effects, and it has thus gradually come to supplant the slower method of chemical responses. Nevertheless the chemical stimulant is still retained, and adrenalin, produced itself by stimulation of the sympathetic, helps to increase the sensitiveness of the response of other parts to sympathetic stimulation. By thus lowering the threshold to sympathetic stimuli, it takes an active part in the preparation for defence. But in addition to this, as Cannon's experiments have shown, adrenalin increases the blood sugar by the liberation of glycogen from the liver, shortens the coagulation time of the blood, and diminishes muscular fatigue, all of which effects are of obvious advantage in the preparation for bodily conflict. As Cannon says (CANNON[24]) "It appears that any high degree of excitement in the central nervous system, whether felt as anger, terror, pain, anxiety, joy, grief or deep disgust, is likely to break over the threshold of the sympathetic division and disturb the functions of all the organs which that division innervates". The mechanism for self-defence which is represented by the sympathetic, has been developed during countless ages from very primitive beginnings, and we may suppose, with Crile, that "we are now in possession of mechanisms which still discharge energy on adequate stimulation, but which are not suited to our present needs". Under conditions of modern life, sympathetic stimulation is not always followed by the bodily activity for which it is intended as a preparation. According to Brown, this may explain some of the phenomena of disease, "and renders intelligible the fact that worry is more injurious than work". (LANGDON BROWN[26]).

The parasympathetic, on the other hand, is mainly anabolic in function. As Cannon says (CANNON[25]) in discussing the cranial outflow - "A glance at these various functions of the cranial division reveals at once that they serve for bodily conservation. By narrowing the pupil of the eye they shield the retina from excessive light. By slowing the heart rate, they give the cardiac muscle longer periods for rest and invigoration. And by providing for the flow of saliva and gastric juice and by supplying the muscular tone necessary for contraction of the alimentary canal, they prove fundamentally essential to the processes of proper digestion and absorption by which energy-yielding material is taken into the body and stored. To the cranial division of the visceral nerves, therefore, belongs the quiet service of building up reserves and fortifying the body against times of need or stress".

The sacral division of the parasympathetic is also concerned in internal service to the body. It causes contraction of the rectum and end part of the colon and also of the bladder, and is chiefly concerned in emptying these viscera. It also includes fibres which bring about engorgement of the erectile tissue of the external generative organs, but have no effect on the internal generative organs (LANGLEY and ANDERSON[27]).

Evidence as to the activity of these two divisions of the autonomic system in disease is suggested by the following list of effects which may be produced by their action, and which are commonly met with in conditions of disease.

Stimulation of the sympathetic division, either general or local, is followed by some or all of the following symptoms: (POTTENGER[28]) Dilatation of the pupil: protrusion of the eyeball: lessened lachrymal secretion: lessened salivary secretion: lessened mucous secretion in nose and throat: lessened secretion in gastro-intestinal tract (hypochlorhydria and retarded digestion): lessened motility in the gastro-intestinal tract, showing as a slowness in the peristaltic wave, contraction of sphincters of the gut, and a general relaxation of the intestinal musculature leading to limited dilatation and to the common type of constipation found in acute infectious diseases: rapid pulse, and at times rise of blood pressure; increase in glycogen content of the blood: increase in body temperature due to (i) an increased production of heat resulting from increased chemical action, (ii) decreased elimination due to vaso-constriction in superficial vessels: diminution in the amount of urine: contraction of the ureter: contraction of the uterus; gooseflesh and increased sweating.

Stimulation of the parasympathetics is accompanied by some or all of the following symptoms met with in disease (POTTENGER[29]). Contraction of the pupil; widening of the eyeslits;

increased lachrymation; increased secretion of nasal, oral and pharyngeal mucous glands (catarrh); increased salivary secretion; contraction of laryngeal muscles such as is met with in laryngeal spasm; increased bronchial secretion, as in bronchitis; spasm of bronchial musculature, as in asthma; hypermotility, and hypersecretion of the gastric glands, including that of hydrochloric acid; hypersecretion and hypermotility of the intestine, leading to colicky pains and states of either spastic constipation and stasis, or diarrhoea, depending much on the degree of stimulation, and whether the circular or more longitudinal fibres are the recipients of the increased stimulation; irritable bladder; incontinuence of urine and faeces.

THE AFFERENT SIDE OF THE AUTONOMIC SYSTEM.

When we come to consider the afferent side of the involuntary nervous system, we are at once met by serious difficulties. It is certain that there is an afferent system, probably as large, and certainly as important as the efferent side, but its experimental investigation is much more difficult. Stimulation of the peripheral cut end of a motor nerve to muscle or gland produces easily demonstrable effects from which inferences may be drawn as to the functions of the nerve. Stimulation of the central cut end of a sensory or afferent nerve may result in reflex production, or it may have no effect whatever that we are able to detect. An adequate stimulus for many sensory nerves cannot be produced without the aid of the peripheral sense organ; and even if it could, the demonstration of the effect produced in consciousness is not possible by laboratory methods. Hence our knowledge of the afferent side of the nervous system is at present very incomplete. According to Langley, a visceral nerve such as the hypogastric, contains in its medullated fibres about ten per cent of afferent fibres, these being of a larger calibre than the efferent, and having their cell stations in the posterior root ganglia.

At each end of the alimentary canal, afferent visceral fibres become much more numerous to allow of the numerous co-operative somatic reflexes associated with these parts (STARLING[30]). The nervus erigens contains about thirty per cent of afferent fibres, and the vagus also carries numerous afferent fibres from the lungs, heart and other organs innervated by it (CHASE[31], EDGEWORTH[32], BARRATT[33]). Most of the fibres are probably connector in function, but there are also afferent neurones and even some sympathetic fibres (MILLER[34]). Similarly a sympathetic nerve in the abdomen may consist of pre- and post-ganglionic fibres, fibres to muscles, bloodvessels and glands, and even sensory fibres belonging to the central nervous system (ALVAREZ[35]). It is extremely difficult, then, to separate out from this maze, those fibres which have afferent functions and to elucidate the exact nature of such functions, and our knowledge of such nerves is as yet very scanty.

In the case of the stomach, Miller has shown that the afferent fibres concerned in the production of reflexes by irritation of the gastric mucosa are conveyed by the vagus and not by the sympathetic. His experiments were performed on cats, and after isolating the vagi and splanchnic nerves, he found that the introduction of warm mustard solution into the stomach, led almost immediately to an increase in the rate and force of the respiration and that tongue and swallowing movements accompanied by salivation were induced, while after an interval of one to three minutes, typical vomiting movements ensued. If now the splanchnics were divided, vomiting could still be induced. Division of the vagi on the oesophagus, however, abolished this power of reflex vomiting. In other similar experiments it was found impossible to induce vomiting after division of the vagi, with the splanchnics intact (MILLER[36]). Miller showed also that stimulation of the trunk of the vagus or of the dorsal or ventral branches to the stomach was also capable of producing vomiting, but he was unable to demonstrate that the splanchnics transmit sensory impulses of any kind from the gastric mucosa. The afferent sympathetic fibres end apparently in the sensitive muscular coat, and these fibres are probably concerned in the conduction of painful stimuli; whereas the afferent vagal fibres, which do not convey painful stimuli, end in the insensitive mucous membrane (HURST[37]).

THE PRINCIPLE OF THE REFLEX ARC IN THE PRODUCTION OF SYMPTOMS.

Sir James Mackenzie first suggested that many of the common symptoms of disease may be explained as disturbances of normal reflex processes occurring in the body (MACKENZIE[38]). The earliest evidence of disease is usually furnished by subjective symptoms, and these involve, in their production, the action of the nervous system.

The nervous system, like other organs, is built up of individual units, and the anatomical unit is the neurone - the nerve cell with its axis cylinder and dendritic processes. The nervous system consists of chains of such units, and the nature of the connection between individual units has been the subject of much controversy. The generally accepted view is that the individual neurones, at all events in the mammal, do not blend with one another anatomically, but are separated by a minute interspace, the synapse, which interspace contains a material with specialised and highly important functions. In the case of invertebrate animals, there is strong evidence in favour of the view of continuity of neurofilrillae from sensory surface to re-acting tissue; and some observers, especially Apathy, Bethe and Held, believe that the same holds true in the nervous system of mammals. Even if this were the case, it would not in any way minimise the importance of the neurone theory, but most observers agree that at the synapse, in vertebrates, there is a break in the continuity of the conducting tissue. This view receives strong support from the Law of Forward Direction - the fact that an impulse will pass from an axon to the next neurone, but will not under any circumstances pass backwards across the synapse from the cell body to the contiguous axon (STARLING[39]).

Nerve impulses may be extinguished at the synapse - never in the neurone itself - and there is always a certain resistance or "block" to the passage of an impulse across a synapse; the impulse is always delayed at ~~its~~ THIS point. Under conditions which produce fatigue, this block or resistance can be markedly increased, while by means of strychnine it can be equally markedly diminished. In an animal poisoned by strychnine it can be shown that every single nerve fibre can set in action every motor neurone of the cord. In such an animal, the slightest stimulus applied to any part of the skin, may excite strong tonic spasms of the whole musculature of the body.

The synapse is also peculiarly susceptible to the effects of education. Passage of an impulse across a synapse or a series of synapses in the central nervous system, if too frequently repeated, leads to fatigue; if, however, the stimulus be not too excessive, and not too frequently repeated, the effect is to diminish the resistance, and to facilitate the passage of the impulse - a process of great importance in the development of "long paths", in the central nervous system. The process of education consists essentially in the laying down of such nerve channels in the still plastic central nervous system, combined with inhibition, by pain, of unfit paths. The process of facilitation is the neural basis of memory itself (STARLING[40]).

The neurone is the anatomical unit of the central nervous system, but it does not appear to be the physiological unit. The latter consists of at least two neurones with an intervening synapse; one of these neurones must be an afferent one, with a specialised end organ or receptor. Stimulation of this receptor results in a nerve impulse which is transmitted along the neurone to the synapse, whence it passes to the second or efferent neurone. The latter conducts it to the end organ or 'effector' organ, which responds by the particular form of physiological activity for which it has been adapted. Between the effector organ and the ending of the efferent neurone, there is another minute interspace occupied by a material with properties very similar to those characteristic of the synaptic membrane. This arrangement of two anatomical units constitutes the basis of the functional unit or "reflex", and the reactions of the nervous system are built up of such units or "reflexes".

The simplest form of a reflex arc is illustrated in Fig.2. A stimulus arising at the sensory surface A is transmitted to the central nervous system where it is 'reflected' at B to produce an end result in a contraction at C. The end result of a reflex, of course, need not necessarily be a contraction of muscle. It may be an inhibitory effect. The effector organ, again, instead of muscle, may be a gland, and as Mackenzie points out, it may be the sensorium (MACKENZIE[41]). Thus in Fig. 2, a stimulus applied to the receptor at A enters the central nervous system as before, is reflected at D. and produces an end result in the

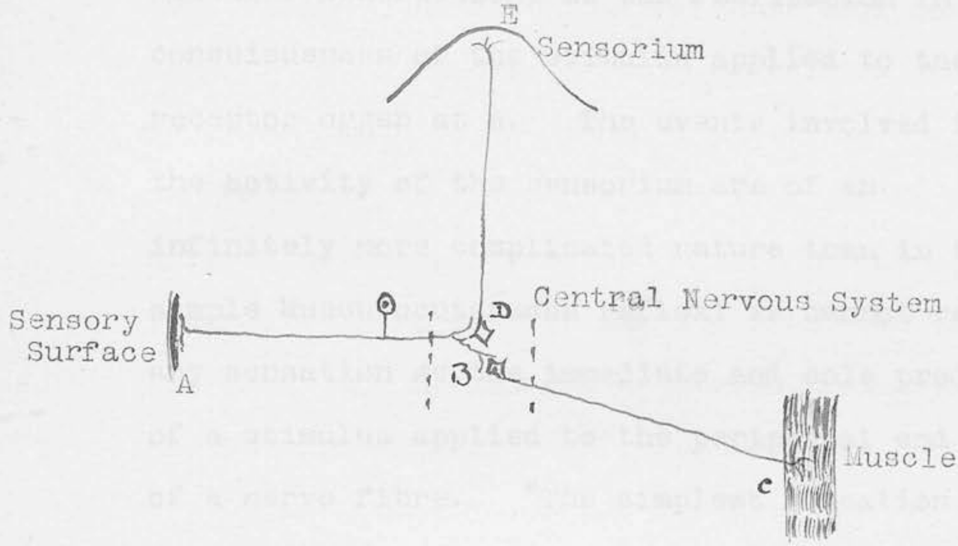


Fig. 2.

Diagram of a Simple Reflex Arc.

sensorium at E; a process exactly comparable with the preceding one, the difference being that in this case, the end result, instead of a muscular contraction, is the realization in consciousness of the stimulus applied to the receptor organ at A. The events involved in the activity of the sensorium are of an infinitely more complicated nature than in the simple Musculocutaneous reflex: we cannot regard any sensation as the immediate and sole product of a stimulus applied to the peripheral end of a nerve fibre. "The simplest sensation involves a judgment i.e. complex neural activities which are the resultant of innumerable past and present streams of nervous impulses aroused by peripheral events, and poured into the central nervous system"(STARLING[42]) Sensation implies consciousness, and of the means by which consciousness is achieved we are wholly ignorant: but we do know that the sensorium is affected and set in action by nerve impulses reflected into it in the same way as the muscle is affected by impulses reflected into it from a sensory surface, and the analogy is therefore sufficiently complete.

The function~~s~~ of the neurone is to conduct nerve impulses in response to stimulation. But "the nervous system is more than a highly elaborate conducting mechanism. The neurone conducts, but it manifests some degree of energy in doing so, though the amount of that energy is very small. There is no evidence that under normal conditions the nerve impulse dies down or undergoes a decrement in the neurone . . . on the other hand nerve impulses set up in an afferent neurone may spread widely in the central nervous system, and the total sum of the resulting discharges by the efferent neurones may be greatly increased" (HERRING[43]).

This spreading of the impulses may be seen in nervous individuals, in whom vomiting may be induced by the sight of an accident: we may assume that in these cases, the afferent impulses entering by the organs of special sense cause a psychic state giving rise to fresh impulses which eventually arrive at the vomiting centre in the medulla, whence they are widely distributed to the various muscles concerned in the act of vomiting. It is obvious, in such a case, that the sum total of the efferent nerve impulses is considerably in excess of the afferent impulses which originate them. The same thing is seen in an exaggerated degree in an animal poisoned by strychnine, where an afferent impulse of the slightest intensity may produce widespread convulsions through spreading of the impulse in the central nervous system; but it is not merely in pathological conditions that such spreading of the impulse occurs. On the contrary, it is a normal phenomenon of every-day occurrence. A barefooted individual who treads upon a tin-tack is usually not content with merely withdrawing his toe from the offending stimulus. The response which occurs is a very brisk one, involving contractions in many muscles of the limbs and trunk, in the muscles concerned in respiration, and probably those of facial expression and of speech. Moreover it is not only in the case of painful stimuli that such spread of the afferent impulses occurs. In violin or pianoforte playing, and in skilled movements generally, many of which are of the nature of reflexes, the sum total of the nervous discharges producing the movement is much greater than that of the afferent impulse which provokes them.

Reflexes exhibited by the decerebrate animal differ in many cases from those shown by the normal animal. In the former case, where the influence of the cerebral hemispheres has been removed, the reflexes that can be obtained are unconditioned; that is to say, the site and the nature of the stimulus being known, it is possible to predict with certainty the character of the response. In the case of the normal animal, when the path of the reflex traverses the cerebral hemispheres, such prediction is not possible. Owing to the multiplicity of tracts open to the impulse in these higher levels, and the various forms of inhibition to which it is subject, the end result of the reflex is not dependent merely on the site and nature of the stimulus applied at the periphery, and the reflex becomes a "conditioned" one. Instances of such conditioned reflexes have already been noted in connection with Pavlov's experiments on the salivary secretion in dogs. If a hungry animal is shown food, there is a reflex secretion of saliva, which in the case of an animal with a salivary fistula, can be collected and measured. If now the giving of food to the animal be always accompanied by some form of stimulus such as the sounding of a definite musical note, the exhibition of a brilliant colour, or the application to the skin of an electric current, it is found after a time that the stimulus becomes effective by itself in producing a reflex flow of saliva (PAVLOV[44]). If, for instance, the dog be allowed to hear two musical notes, say middle C and middle C#

at frequent intervals, and the former be always followed up by the presentation of food, it can be shown in a few days that not only can he distinguish between the two sounds, but that he has a memory of the absolute pitch. When the note middle C is sounded a flow of saliva occurs, whereas the C## produces no such flow. The afferent path for this acquired reflex must pass through the higher cortical centres, where it is subject to various forms of inhibition, and is therefore 'conditioned'.

It is found that in the higher animals, many reflexes tend to take the long path through the cortex rather than the shorter ones direct through the cord. Thus in man, in cases of fracture of the spine, the part of the cord below the lesion fails for some time to act as a reflex centre, and it only slowly acquires the ability to function in this way. This delay in the appearance of reflexes is due partly, no doubt, to shock, which, however, passes off after a period of one to three weeks. After this time, certain of the reflex functions of the cord return, but not so completely as in the case of the lower animals. The higher the animal in the organic scale, the more do the reflexes tend to be promoted to the higher levels of the central nervous system. In the spinal man, almost any stimulus, if of sufficient intensity, tends to result in a "mass reflex". The nicely graduated response to stimulation which we find in lower animals is absent, and in its place we get flexion of both legs combined with contraction of the abdominal muscles and frequently profuse sweating over all those parts of the body below the level of the injury. Extensor reflexes are not obtained, owing to the transference of the postural reflexes to the jurisdiction of the upper parts of the central nervous system (STARLING[45]).

Various observers have shown at different times that it is possible to obtain, by varying certain conditions, a reversal of the reflex results ordinarily produced by afferent stimuli. Thus Bayliss showed many years ago that by means of chloroform the reflex effect obtained by stimulating afferent nerves in the rabbit can be changed from a rise of blood pressure into a fall (BAYLISS[46]). He showed, further, that in the rabbit, chloroform alters reflex excitation of vaso-constrictor nerves into reflex inhibition (BAYLISS[47]). The effect of strychnine in the reversal of reflexes has already been referred to. Sherrington, in studying the reflexes in skeletal muscle, found that reflexes having an inhibitory effect on the knee extensor muscle in the cat and dog were changed by a small dose of strychnine so as to become excitatory instead of inhibitory, and induced contraction instead of relaxation of the muscle (SHERRINGTON[48]). He showed, further, that this effect could be undone again by a sufficient dose of ether or chloroform, so that the effect of the stimulus becomes inhibitory once more; and by increasing or diminishing the dose of chloroform the effect can be changed from excitatory to inhibitory and back again several times in succession. A similar action of strychnine in reversing the blood pressure reflexes in the rabbit has been demonstrated by Bayliss (BAYLISS[49]). Sherrington and Sowton carried the investigations still further in the case of chloroform. They found, first, that in a decerebrate preparation of the cat, where the knee extensor (vasto crureus) exhibits marked tone, weak stimulation of various afferent nerves of the ipsilateral limb produces in many cases a reflex contraction of the muscle; whereas with a stronger stimulus, a reflex inhibition is produced (SHERRINGTON and SOWTON[50]). Working with preparations which gave these reactions, these authors found that by merely increasing the dose of chloroform, they could change the effect of the given stimulus of constant intensity from excitation and contraction into inhibitory relaxation (SHERRINGTON and SOWTON[51]). Thus by merely altering some one definite factor in the conditions of the reaction, it is possible to reverse the effect of the reflex obtained from stimulation of an afferent nerve. Sherrington and Sowton separate these changes of reaction into two groups, according as (1) the determinant alteration lies in conditions attaching purely to the stimulation of the afferent paths, or (2) to some other part of the reflex, for example the central mechanism. In the former group is the change of movement of the hind limb of a spinal dog from flexion to extension when the stimulus applied to the sole is changed from a nociceptive to a tactual one innocuous in character (SHERRINGTON and SOWTON[52]). In the second class of reversals the result is not dependent on any change either of intensity or quality in the stimulus, but depends on conditions affecting, probably, the central mechanism. Thus the reflexes obtained in a limb from identical stimuli may be diametrically altered by a passively imposed change in the posture of the limb, and Magnus has traced this result to an influence exerted by the change of posture upon the central mechanism of the reflex (MAGNUS[53]). To the second group also belong the reversals effected by poisons such as strychnine and chloroform. These drugs probably produce their effects, in the cases we have been considering, by action on the nerve synapses. It is possible that many other substances have similar properties in interfering with the innumerable reflex processes constantly occurring in the body, and some symptoms of disease may be produced by disturbances of reflexes initiated in this way.

No neurone has the property of initiating nerve impulses on its own account; at all events it has never been proved that any neurone or system of neurones has the power to do so. It would be highly undesirable for afferent neurones to possess the property of automaticity, and as a matter of fact, they do not. It is also highly improbable that efferent neurones possess such a property, although attempts have been made to prove that they do e.g. in the case of the efferent neurones of the respiratory centre. It is impossible, however, to cut off such a centre from all afferent impulses, and no attempt to prove the automaticity of the centre has been successful. Furthermore we know that the material in the synapse is extremely sensitive to the action of chemical agents, and it is possible that some of the synapses in the respiratory centre are especially susceptible to hydrogen ion changes in the tissue fluid in the vicinity, and that the rhythmic actions of the centre can be explained in this way (HERRING[54]).

Another property of neurones (and, indeed, of all living cells) which has important bearings on the study of symptoms of disease has been demonstrated by the St. Andrew's Institute for clinical research. This is the property of 'fluctuation', (HERRING[55]). The skin is the tissue in which this property can be most easily demonstrated. In examining patients with hyperaesthesia of the abdominal wall from visceral disease, or of the chest wall from heart disease, one is never able to map out sharply the edge of the hyperaesthetic area. Small areas of skin which are sensitive to slight stimuli at one moment, are found insensitive the next, and vice versa. Similarly in the healthy skin, small spots can be found which are sensitive to heat and cold, and other spots which are insensitive, and it is found that these spots vary in the same way, the sensitive ones becoming insensitive and vice versa, (WATERSTON[56]). These results are explained as being due to alternate periods of activity and quiescence in the neurones concerned: and it is frequently possible to demonstrate similar fluctuation in the calibre of the skin capillaries (MACKENZIE[57]). It is probable that the phenomenon of fluctuation is a universal one in living tissues, and it is a phenomenon of considerable importance. It enables us, for instance, to understand the possibility of a graded response to stimulation in such an organ as the heart. Since the response of the neurone to stimulation is an "all or nothing" one, and it is not possible to vary the strength of the impulse in the individual neurone, the explanation of the graded response of the stimulated organ must be sought for in the varying number of neurones taking part at any one time in the stimulating process.

THE SECRETION AND INNERVATION OF THE GASTRIC GLANDS.

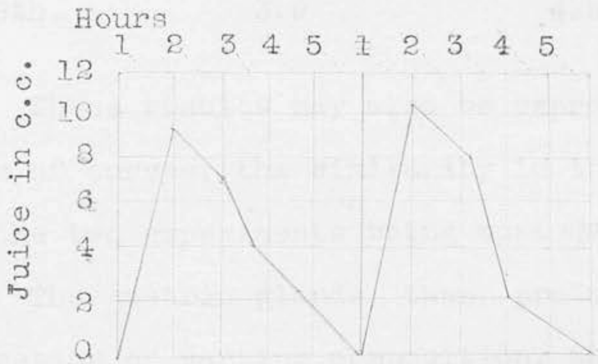
The glands of the stomach, like other organs, are thrown into activity only on receipt of an adequate stimulus. In the case of the gastric glands, the necessary stimulus is provided by the introduction of food into the alimentary canal. Pavlov and his co-workers in Russia were the first to demonstrate the extremely purposive nature of the response of the gastric glands to such stimulation. They showed, for instance, that the secretion of the glands varies directly in amount with the amount of food taken; it varies also, both in amount and in quality (ferment content), with the kind of food on which it is poured out.

In the investigation of these points, Pavlov devised an ingenious operation, by means of which a small diverticulum is formed at one end of the stomach, in direct muscular and nervous continuity with the rest of the organ, but cut off from the main part of the viscus by a diaphragm of mucous membrane. The diverticulum, or miniature stomach, represents about one tenth of the capacity of the whole organ, and Pavlov was able to show that the secretion in the miniature stomach was an accurate reflection of that occurring in the large stomach. Both in quantity and quality, the juices from the two parts of the organ run parallel to one another.

Working with animals operated on in this way, Khizin, in Pavlov's laboratory, found the following average amounts of juice secreted on given quantities of food; for 100 grms. of flesh, 26.0 c.c. of juice were secreted; for 200 grms. 40.0 c.c.; for 400 grms. 106 c.c. with a mixed diet of 50 grms. meat, 50 grms. bread, and 300 c.c. of milk, 42.0 c.c. of juice were secreted. With double these quantities, 83.2 c.c. These figures show a definite ratio between the amount of food introduced and the amount of juice secreted (PAVLOV[58]). Furthermore, the secretion occurs in a certain definite manner for the various kinds of food; the rate of secretion and the digestive power of the juice secreted vary in a definite way according to the kind of food undergoing digestion. The following table (PAVLOV[59]) shows the hourly variation in quantity of juice after a meal of 100 grammes of flesh. Two experiments are recorded.

Hour after feeding.	Quantity of juice in c.c.	
1st.	11.2	12.6
2nd.	8.2	8.0
3rd.	4.0	2.2
4th.	1.9	1.1
5th.	0.1	a drop
	Total 25.4	23.9

These results may be expressed also in the form of curves. With meat, the curve of secretion rises rapidly to a maximum during the first hour, and then gradually falls till the secretion ends, after five hours. Different kinds of food, as Pavlov's experiments indicate, give different and characteristic curves of secretion, showing that the glands vary their product quantitatively with the particular kinds of food. But furthermore the quality of the juice varies also in a very definite manner. The following table from Pavlov (PAVLOV[60]), shows the hourly variation in digestive power of gastric juice in dogs, after a meal of 400 grammes of raw flesh, the digestive power being estimated by Mett's method - the number of millimetres of coagulated egg-white (contained in capillary



Curve of Secretion of Gastric Juice after a meal of flesh.

(Two Experiments)

Pavlov. 'The Work of the Digestive Glands'. p. 26.

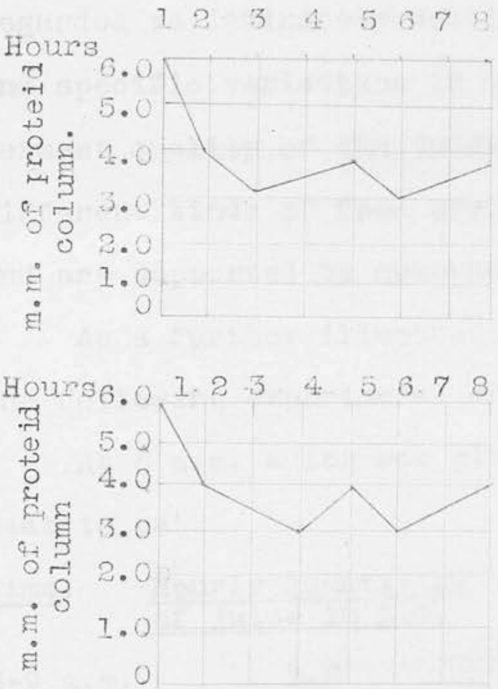
tubes of standard diameter), dissolved in a given time.

Hour	Millimetres of egg-white column digested.	
1st.	6.0	5.8
2nd.	4.3	4.1
3rd.	3.4	3.4
4th.	3.5	3.0
5th.	3.8	3.8
6th.	3.0	3.1
7th.	3.6	3.5
8th.	3.9	4.5

These results may also be expressed in the form of curves, the similarity in the curves of the two experiments being most striking (Fig. 4)

The gastric glands, then, produce a secretion of varying composition, and one which fluctuates in quantity according to definite laws. The strength of the secretion (the amount of ferment it contains) does not depend on the quantity of the juice - the secretion when copious may be of strong or weak digestive power, and similarly when it is scanty. The two properties, quantity and quality vary independently of each other, and according to the needs of the particular food undergoing digestion. According to Pavlov, however,

Fig. 4.



Digestive power of hourly portions of gastric juice after administration of 400 grammes of flesh.

(Two experiments)

Pavlov 'The Work of the Digestive Glands'. p.31.

the gastric juice as it flows from the glands, possesses a constant acidity (PAVLOV[61]). Observations to the contrary he explains as being due to various degrees of neutralisation of the juice by the alkaline mucus of the stomach, or by admixture with alkaline saliva in food. This is a point which cannot be regarded as definitely settled, but the definite and specific variations in the quantity and ferment quality of the juice provided for different kinds of food are most striking, and are supported by numerous experiments.

As a further illustration Pavlov quotes the following experiments of Khizin (PAVLOV[62]):-

At 8 a.m. a dog was given 200 grammes of meat to eat.

Time.	Hourly quantities of juice in c.c.	Digestive power in m.m.
8-9 a.m.	3.2	8.0
10 "	4.5	7.0
11 "	1.8	7.0
The dog was now given 200 grammes of raw meat.		
12 noon	8.0	5.37
1 p.m.	8.8	3.50
2 "	8.6	3.75
The dog now received 200 c.c. of milk.		
3 p.m.	9.2	3.75
4 "	8.4	3.30

An additional quantity of 400 c.c. milk was now given.

Time.	Hourly quantities of juice in c.c.	Digestive power in m.m.
5 p.m.	7.4	2.25
6 "	4.2	2.2

These results show that the farinaceous food calls forth a relatively scanty flow of juice, which, however, is of high digestive power. Meat produces a free flow of juice of rather smaller enzyme content, while milk provokes also a free flow of secretion, which, however, is of very low digestive power.

The qualitative and quantitative variations in the juice secreted hour by hour on these different kinds of food is illustrated in the following table from Pavlov.

Quantities and properties of gastric juice poured out on different diets:- 200 grms. flesh, 200 grms. bread, 600 c.c. milk.

	Quantities of Juice in c.c.			Digestive power in m.m.		
Hour.	Flesh,	Bread,	Milk,	Flesh,	Bread,	Milk.
1st.	11.2	10.6	4.0	4.94	6.10	4.21
2nd.	11.3	5.4	8.6	3.03	7.97	2.35
3rd.	7.6	4.0	9.2	3.01	7.51	2.35
4th.	5.1	3.4	7.7	2.87	6.19	2.65
5th	2.8	3.3	4.0	3.20	5.29	4.63

Hour.	Flesh.	Bread.	Milk.	Flesh.	Bread.	Milk.
6th.	2.2	2.2	0.5	3.58	5.72	6.12
7th.	1.2	2.6		2.25	5.48	
8th.	0.6	2.6		3.87	5.50	
9th.		0.9			5.75	
10th.		0.4				

These figures show that flesh produces its maximum secretion in the first or second hour of digestion (in dogs) while the digestive power of the juice is also strongest in the first hour. Bread gives a pronounced maximum of secretion in the first hour, but the juice is strongest in the second and third hours. Milk produces the maximal flow of juice in the second or third hour, but the maximal strength is in the last hour of digestion. It is obvious that these differences are not merely accidental. Their purposive nature is well shown in the case of the farinaceous diet, where as we have seen, the pepsin content of the juice is high, but the total amount of the juice relatively small. In this way an excess of acid is avoided; and as the presence of much acid hinders starch digestion, the advantage of this, as Pavlov points out, is obvious. Further, the relatively small amount of acid secreted for the farinaceous food allows of the more ready escape of the latter into the next part of the alimentary canal, where the main processes in its digestion occur. With meat, the larger amount of acid secreted not only closes the pylorus from the gastric side, but also requires more time for its neutralisation in the duodenum, and hence the escape of the meat from the stomach is slower - the pylorus being kept closed by the acid in the duodenum (CANNON[63]). Thus more time is allowed, in the case of meat, for the digestive processes to continue in the stomach; a purposive arrangement of considerable importance, as an essential part in protein digestion is played by the gastric juice.

We have seen that the stomach receives nerve fibres from the vagus and from the sympathetic nerves; and the question arises as to whether the activities of the gastric glands are in anyway regulated by these nerves. Pavlov first threw light on the subject by his experiment of "sham feeding" or "fictitious feeding". In a dog provided with a gastric fistula, he divided the oesophagus and brought the cut ends to the surface, so that food eaten by the animal did not reach the stomach, but dropped out at the opening in the neck. Nevertheless he found that in such animals the giving of food was invariably accompanied, after a latent period of five minutes, by the appearance of gastric juice in the stomach; and the flow of juice, once established, continued as long as the animal continued eating. Some of his dogs would persevere in the attempt to satisfy their hunger for as long a period as five or six hours; during which time as much as 700 c.c. of gastric juice were produced, without any food whatsoever entering the stomach (PAVLOV[64]). It is obvious that the stimulus to the glands in this case must be of a nervous nature. Pavlov proceeded next to divide the right vagus below the level of the cardiac and pulmonary branches, in a dog with a gastric fistula. Sham feeding, as before, produced a copious flow of juice. If now, however, he cut the left vagus in the neck, so isolating the stomach from all vagus influence, sham feeding had no effect on the production of gastric juice. The dog would accept food and eat it greedily, but not a drop of gastric juice resulted (PAVLOV[65]). These experiments furnished practically conclusive evidence of the presence in the vagi of secretory fibres to the gastric glands. Final and decisive evidence was afforded by the effect of rhythmic excitation of the cut nerve, (excitation by slow induction shocks at intervals of from one to two seconds), when, if the experiment was performed without pain or discomfort to the animal, a secretion of juice was obtained from the empty stomach. It was necessary always to observe the condition of absence of pain or fright on the part of the animal, as these conditions of themselves inhibit the production of gastric juice. Netschaiev, for instnace, found that excitation of the sciatic nerve for two or three minutes was able to stop gastric digestion for several hours (PAVLOV[66]).

These experiments, then, demonstrate the presence in the vagi, of secretory fibres to the gastric glands. The effect of the sham feeding, however, does not depend on simple reflex processes from the cavity of the mouth playing upon the secretory nerves of the stomach. If this were the case, any substance applied to the buccal mucous membrane which called forth a secretion of saliva, should also reflexly cause a secretion of gastric juice. This is found not to be the case. For instance, acid in dilute solution applied to the mouth is a most effective agent for the production of saliva. It has no effect whatsoever on the secretion of gastric juice. Pebbles may be given to the dog to swallow (which, with a little training, he will readily enough do) with a similar absence of result on the gastric glands (PAVLOV[67]). Thus neither chemical nor mechanical stimulation of the buccal mucous membrane can reflexly excite the nerves of the stomach. Further, owing to the long pause, (five minutes) between the chewing and swallowing of food in sham feeding, and the appearance of gastric juice, it is evident that the excitation of the gastric nerves is not due to simultaneous stimulation of the secretory centre of the gastric glands from the mere excitement of chewing and swallowing. The animal goes through the movements of chewing and swallowing pebbles, without any formation of gastric juice as a consequence.

Everyone knows how, in a hungry individual, the mouth "waters" at the sight of appetising food. Pavlov showed that the stomach behaves in a similar way, (PAVLOV[68]) and the flow of gastric juice observed in sham feeding experiments is due to the psychic effect aroused by the sight of food. It is not necessary actually to give the dog food to chew; the mere preparation of food in front of the animal is sufficient to arouse his interest, to stimulate his appetite, and to produce a brisk flow of gastric juice. Pavlov quotes the following experiment of Sanotskii, in which the secretory effect of the sight of food is compared with that of sham feeding. (PAVLOV[69])

Duration of Flow.	Quantity of Juice.
8 minutes.	10 c.c.
4 "	10 "
4 "	10 "
10 "	10 "
10 "	10 "
8 "	10 "
8 "	10 "
19 "	10 "
19 "	3 "

Then followed a sham feeding for six minutes

17 minutes	10 c.c.
9 "	10 "
8 "	10 "

It is obvious that in this experiment the psychic effect is equal to, or exceeds, that of the sham feeding. The psychic effect is also responsible for variations in the amount of juice with variations in the nature of the food. The greater the relish shown by the animal for the food, the greater the quantity of juice secreted. Thus if the dog is given pieces of boiled meat of a definite size at definite intervals, the resultant juice is scanty, the latent period prelonged, and after a comparatively short time the animal ceases to eat. If now, as soon as the flow of juice ceases, corresponding pieces of raw meat are given at corresponding intervals the animal eats greedily (and may do so for hours), the flow of juice begins promptly at the end of five minutes, and is much more copious in amount (PAVLOV[70]). In a dog which prefers boiled to raw meat, the reverse occurs. In most dogs, meat produces more juice than bread; but in dogs which prefer meat to bread as a food, the former is more effective. Milk produces but a scanty flow of juice, and these differences in the amount of juice occur in juice secreted at the sight of food, as well as that resulting from sham feeding (PAVLOV[71]). It is obvious from these experiments that the first step in the process of digestion depends on a highly complicated reflex; the simultaneous stimulation of the senses of sight, hearing, smell and taste causes a psychic state resulting in stimulation of the secretory nerves to the gastric glands. This psychic state is the condition known as appetite; and the possession of a healthy appetite, therefore, appears to be a necessary condition for the normal performance of the first processes of digestion. This, however, is not the whole story of gastric digestion. In the course of his experiments Pavlov found that when an animal was given a normal meal and allowed to swallow it in a normal way, the amount of gastric juice secreted was more than that obtained from a sham feeding of the same amount of food. Sham feeding, also, results always in a digestive juice of the same digestive power, and the same percentage of hydrochloric acid, no matter what the previous diet of the animal may have been; whereas we have already noted the differences that occur in gastric juice poured out on food that has been actually swallowed. We must conclude that the gastric juice consists of two parts (1) A larger portion, the appetite juice, produced reflexly by the psychic state already considered, and (2) a smaller portion, varying in composition with the nature of the food and produced by the stimulus of the food in the stomach. These two portions can be produced separately in dogs provided with a miniature stomach by Pavlov's method, and a fistula into the large stomach. In such an animal, a sham meal will cause a secretion from the miniature stomach, which can be collected and measured. Subsequently, a corresponding amount of food may be introduced direct into the large stomach, when again a flow of juice will occur from the miniature organ. This is best done with the animal sleeping, in order to avoid any possibility of a 'psychic' flow. The total amount of juice obtained from these two experiments is found to agree almost exactly with that produced when the same amount of food is eaten and swallowed in the normal way.

This second portion of gastric juice cannot be ascribed to any action of the extrinsic nervous supply, since it occurs after complete separation of the stomach from the central nervous system. It cannot be due to mere mechanical stimulation, for Pavlov showed most conclusively that mechanical stimulation of the gastric mucous membrane by any means whatever is quite unable to provoke the slightest flow of gastric juice (PAVLOV[72]). Moreover it is not provoked by every kind of food; bread, for instance, or the white of egg do not give rise to any secretion when introduced directly into the stomach. The most potent stimulants for the 'chemical' secretion of gastric juice are meat, and various forms of meat extract. Popielski found that the direct injection of bouillon into the blood stream caused no secretion; and as it provoked a flow when introduced into the stomach after section of both vagi, and destruction of the abdominal sympathetic nerve plexuses, he concluded that it was due to reflex action of the local nerve plexuses. This view involved the assumption of a specific sensibility of the gastric mucous membrane to many ordinarily inert substances; and the discovery of secretin by Bayliss and Starling suggested an alternative possibility. Although the direct introduction of bouillon into the blood stream was powerless to provoke a flow of juice, the possibility remained that on contact with the gastric mucous membrane it may give rise to a substance in the cells of this membrane, which when absorbed into the blood stream acted as a direct excitant to the gastric glands. Such, indeed, has actually proved to be the case. A series of experiments carried out by Edkins has placed the matter beyond doubt (EDKINS[73]). This observer had previously shown that normal saline solution introduced into the stomach would remain there for several hours unabsorbed, and with no change in reaction. In his experiments on gastric secretion, which were performed on cats, he first ligatured the cardiac orifice of the stomach, and introduced a cannula through the duodenum into the pyloric end, tying this in at the level of the pyloroduodenal junction, "The ligature at the pyloric end, was passed beneath the peritoneum, so as not to interfere with any large blood vessels. That at the cardiac end was tied sufficiently tightly to physiologically sever the vagus fibres. The cannula was connected with a reservoir of normal saline solution in such a way that the amount passing into the stomach could be measured, and either a known quantity was first passed into the stomach, or the stomach was dilated to its full capacity by the saline solution being supplied at a certain pressure... The animals were almost invariably used in the fasting state, and the effects are much more obvious in this state . . .

At the end of the different stages of the experiment, the normal saline solution was removed and tested for hydrochloric acid and in many cases, pepsin" (EDKINS[74]).

Using this method Edkins found that the injection of peptone, of acid, of broth or of dextrin into the blood stream caused no secretion; but that extracts made of the pyloric mucous membrane in boiling water or in .4 per cent hydrochloric acid contained an active substance which on injection into the blood vessels caused an active secretion of gastric juice. He found also that extracts made in cold water, peptone, glucose or glycerine also contained variable amounts of this substance; but that extracts of the fundus mucous membrane, however made, do not contain it. The gastric hormone, therefore, appears to be produced only in that part of the stomach where the process of absorption is most marked. As boiling an extract of the pyloric membrane increases rather than diminishes the activity of the substance, Edkins concludes that it is not a ferment; and as its effect in causing secretion is in no way diminished by massive doses of atropin, he infers that it does not act by any excitation of a local nervous mechanism, but directly on the protoplasm of the secreting cells (EDKINS[75]).

We may conclude therefore, that under normal conditions, the gastric glands are thrown into activity at the commencement of a meal by a reflex nervous mechanism through the vagi. This depends, for its successful accomplishment, upon a psychic state, appetite, or the desire for food, produced in turn by stimuli entering through the organs of special sense. The juice provided by this stimulus is of a definite and constant composition, depending on the animal. By the action of this juice on the foodstuffs ingested, substances are formed which affect the cells of the pyloric mucous membrane in such a way that a body, or bodies are produced which are absorbed into the blood stream and act as direct excitants of the gastric glands. In this way provision is made for the continuance of digestion after cessation of the initial stimulus, and also, possibly, for the modification of the gastric juice according to the needs of the particular food undergoing digestion. In the case of foods which do not excite a secretion when introduced directly into the stomach, the "appetite juice" is essential to digestion. Variations in the amount of the chemical juice may also occur from the nature of the salts present in the food and from the amount of fluid available for the formation of gastric juice; but the production of this portion of the gastric juice probably does not depend on any regulation by nervous processes, at all events in a positive direction.

Inhibition of the work of the gastric glands may be produced by painful stimuli and also by emotional states, in which case the cessation of activity is due to a restraining influence exerted by the sympathetic nerves to the glands; impulses which are transmitted outward by the splanchnic nerves - 'the pre-ganglionic fibres that reach to the great ganglia in the upper abdomen, and thence are spread by post ganglionic fibres all along the gut,' (CANNON[76]).

THE MOVEMENTS AND INNERVATION OF THE GASTRIC MUSCULATURE.

In addition to providing the gastric juice for the preliminary digestion of food, the stomach has other duties to perform. It must act as a reservoir for the reception of food, and must be prepared to vary its size with the quantity of food introduced at one time; in many cases it is required to grind the food into smaller particles, and at the same time mix it thoroughly with the gastric juice; and finally it has to arrange for the transmission of the resulting chyme into the next section of the alimentary canal. Still another function appears to be that of calling the attention of the animal to the need for food, as the 'pangs of hunger' apparently depend on muscular contractions in the gastric walls. These various functions and the manner in which they are normally performed may be considered separately.

The entrance to the stomach is guarded by the cardiac sphincter - a thickened band of smooth circular muscle, situated at the gastro-oesophageal junction. This band, in common with the muscle of the oesophagus and the stomach receives nerve fibres from the vagi, and Langley was able to show that these include both motor and inhibitory fibres. Stimulation of the vagus in the neck causes relaxation of the sphincter, followed, after cessation of the stimulus, by strong contraction. Langley introduced a tube into the oesophagus filled with warm saline solution and connected with a manometer, and after injecting curari to paralyse the nerve endings in the striated muscle, and atropine sulphate to weaken the oesophageal motor fibres, he found that stimulation of the peripheral cut end of the vagus caused a sharp fall in the level of the manometer fluid, indicating inhibition of the cardiac sphincter, (LANGLEY[77]) and thus demonstrating the presence of inhibitory fibres in the vagus. Injection of adrenaline caused also marked relaxation of the sphincter, so that inhibitory fibres are supplied also by the sympathetic (LANGLEY[78]).

The two sets of fibres in the vagus are probably called into play during the swallowing of a bolus of food. The inhibitory fibres relax the sphincter to allow entrance of the food; and following this, impulses through the motor fibres cause an increase in the tone of the sphincter (CANNON[79]). The relaxation of the muscular coats of the stomach to receive the food is possibly effected in part by the same mechanism, since the introduction of food into the stomach is not associated with an increase of intragastric tension. Kelling demonstrated this fact, and quotes an experiment in which in a dog with 240 c.c. of liquid in its stomach the intragastric pressure equalled 7.6 c.m. of water. When the quantity was increased to 460 c.c. the pressure recorded was 7.0 c.m. (KELLING[80]). This adjustment, however, does not occur instantaneously. It requires at least one minute for its accomplishment, and since the surviving excised stomach can relax in the same way, the mechanism concerned evidently resides in the wall of the stomach. Under the influence of anaesthetics no adjustment occurs, and the organ can be distended to bursting. Under normal conditions, however, it is possible that the vagi take a part in the process, and Cannon has noted that the act of swallowing is accompanied by a rapid fall of intragastric pressure; an effect mediated through the vagi, since it does not occur if they are cut (CANNON[81]). The cardiac orifice opens as a rule to each ordinary act of swallowing, but if a series of acts be made in rapid succession it remains passively open for some time. On the other hand if the acts of deglutition are weak, it opens only to every third or fourth (PAVLOV[82]). The opening and closing of the cardia is stated by Pavlov to be due to a reflex, the mechanism of which, however, is not clearly understood. Gentle stimulation of the oesophageal mucous membrane leads to opening, as does the presence in the oesophagus of unirritating fluids at or near body temperature. Rough stimulation, and cold or carbonated waters cause contraction. From the lower side, increase of gastric pressure leads to opening; an effect not due merely to mechanical causes, as it does not occur if the animal be narcotised (PAVLOV[83]). An active opening of the sphincter occurs also in vomiting.

These activities of the cardiac orifice are of considerable interest in connection with a very common symptom of "indigestion", viz., re-gurgitation of food from the stomach into the oesophagus. Cannon has demonstrated in cats a rhythmic re-gurgitation of food which depends, apparently, on rhythmic variations in the tone of the cardiac sphincter. In his experiments the animals were given a thin starch paste mixed with bismuth subnitrate, and the movements watched by means of X-rays.

If enough of the fluid was introduced to produce an intragastric pressure sufficient to overcome the resistance of the sphincter, the fluid could be seen to shoot suddenly up into the oesophagus at intervals of fifteen or twenty seconds; each portion as it escaped being seized by a peristaltic wave in the oesophagus and pushed back into the stomach again. Acidulation of the fluid to 0.5 per cent, which is normal for carnivora, stopped this to and fro movement of the food. If the gastric contents were rendered acid, the intragastric pressure could be raised considerably without any escape from the stomach, showing that the acid acts from the stomach side to close the cardiac orifice. Section of the splanchnic nerves had no effect on the regurgitation, but after such section, acidity in the gastric contents lost none of its effect. The closure of the cardia therefore, with increasing acidity, does not depend on any reflex through the sympathetic. Section of the vagi destroys the ability of the oesophagus to exhibit peristalsis, and so obscured the mechanism of the process under consideration; but as the intragastric pressure required to force the cardiac orifice after vagus section was found to be much higher with acid gastric contents than with neutral or alkaline, Cannon concluded that the reflex processes concerned were not mediated by the vagi, and must therefore be relegated to a local reflex mechanism in the wall of the gut (CANNON[84]).

We may conclude then, that under normal circumstances, food approaching the stomach along the oesophagus is allowed to enter by a reflex opening of the cardia, this reflex being mediated by the vagus. The food once admitted, motor fibres in the vagus cause an increase of tone in the cardiac sphincter, tending to prevent regurgitation; and as digestion proceeds, the increasing acidity of the gastric contents acts reflexly through a local nervous mechanism in the wall of the stomach to keep the cardia closed and prevent regurgitation.

The exit from the stomach is guarded by the pylorus, and the opening and closing of the pylorus is regulated by a reflex nervous mechanism in such a way that acid on the gastric side causes opening, while acid on the duodenal side causes closing of the aperture. The evidence for this acid control of the pylorus has been collected by Cannon. (CANNON[85]) It is found that delay in the appearance of acid in the vestibule of the stomach delays the initial discharge of the gastric contents into the duodenum. If an animal is given a meal of carbohydrate mixed with bismuth salts, and the discharge of the gastric contents watched by means of X-rays, it is found that the escape begins quickly, usually within ten minutes, and the amount of food discharged rises rapidly to a maximum in two hours. If now the same meal be given, but moistened with sodium bicarbonate, there is a very marked retardation in the escape (CANNON[86]). As the sodium bicarbonate not only neutralises the hydrochloric acid secreted, but also inhibits the secretion of acid (PAVLOV[87]) this observation tends to show that absence of acid in the vestibule is associated with delayed opening of the pylorus.

Protein food, which undergoes important digestive changes in the stomach, does not leave that viscus nearly as rapidly as carbohydrate food (CANNON[88]). If, however, the protein is first digested by acid until converted to acid protein and the free acid dialyzed away, feeding the acid protein to an animal is followed by a very speedy exit from the stomach. In half an hour, five to ten times as much acid protein is discharged from the stomach as in the case of natural protein (CANNON[89]). As natural protein has considerable powers of combining with hydrochloric acid, while acid protein, of course, has none, this observation also lends considerable support to the view that free acid on the gastric side of the pylorus facilitates the opening of the latter. Furthermore, on making a fistula into the vestibule of the stomach, so that portions of the vestibule contents could be removed from time to time and the presence or absence of acid determined, Cannon found that the initial discharge of the food through the pylorus was always accompanied by an acid reaction of the food in the vestibule, which previous to such discharge always showed an absence of free acid. Finally Cannon performed an interesting experiment which not only gave strong support to the theory of acid control of the pylorus, but also showed that such control could be exerted independently of any connection with the central nervous system. A fasting cat was quickly killed by etherisation. The empty stomach was then removed and placed in warm oxygenated Ringer's solution. A glass tube, with a short rubber tube and a water manometer attached, was tied into the cardiac orifice. A small amount of 0.4 per cent hydrochloric acid, coloured blue by an indicator (Congo red) was next introduced through the tube into the fundus, which was held lower than the vestibule. The stomach was then inflated with air until bubbles escaped through the pylorus, when the rubber tube was tightly clamped. When the air had ceased to escape through the pylorus - showing that the latter was closed - the stomach was gently and slowly turned until the acid came to the pylorus. "In a moment the blue fluid poured forth into the Ringer's solution. The pylorus had opened." (CANNON[90]). In a control experiment with a coloured alkaline solution, the fluid did not emerge for a considerably longer time, and then only slowly diffused out. The evidence seems fairly conclusive that acid on the gastric side of the pylorus will open the sphincter, and that it can do so without any assistance from the extrinsic nerves.

Evidence as to the closure of the pylorus from the duodenal side was produced by Serdjukow, working in Pavlov's laboratory. He showed that by the introduction from time to time of acid solutions or gastric juice into the duodenum, discharge from the stomach could be prevented for an unlimited time. Pavlov also noted that in dogs with a pancreatic fistula, and in which, therefore, the normal alkaline juices of the duodenum were absent or diminished in amount, acid solutions left the stomach much more slowly than usual; (PAVLOV[91]) an observation which Cannon confirmed and extended by cutting through the intestine of a cat about 1.5. cm. beyond the pyloric furrow, and again about 30 cm. beyond. The upper end of this separated portion he turned in and closed with stitches; the lower end he joined to the gut near the ileocolic opening by an end to side junction. Finally he united the upper end of the main part of the intestine to the small remnant of duodenum contiguous to the pylorus, so that the stomach emptied not into the duodenum, but into a part of the intestine previously thirty cm. further on. In animals operated on in this way, he found a remarkable increase in the rate at which foods left the stomach; (CANNON[92]) the restraining effect of acid in the duodenum being absent, the acidity on the gastric side operated unchecked to open the pylorus and allow the escape of the gastric contents.

We must conclude that normally the discharge of the stomach contents into the duodenum is regulated by stimuli arising from the presence of free acid, and operating in two ways; free acid in the vestibule causes a reflex opening of the pylorus and consequent escape of the gastric contents into the duodenum; and free acid in the duodenum causes a reflex closing of the sphincter; an arrangement remarkably in harmony with Bayliss and Starling's Law of the Intestine, that a stimulus causes contraction above and inhibition below the stimulated area. This reflex mechanism can operate independently of the extrinsic nerve supply, and must therefore depend on the local reflex centres in the bowel wall. In order to determine the exact path of the reflex, Cannon made a circular incision round the intestine immediately beyond the pylorus, and deep enough to sever both muscular coats, leaving intact only the mucosa and the submucous connective tissue. The effect of this procedure on the exit of food from the stomach was almost the same as when the duodenum was completely set aside; showing that the paths of the reflex involved had been severed (CANNON[93]). Cannon infers, therefore, that the influence from duodenum to pylorus runs through a local reflex, mediated by the myenteric plexus.

The movements of the stomach walls are best studied by means of X-ray observations on living animals; a method of investigation which in the hands of Cannon has yielded valuable information. Anatomically the body of the stomach is marked off from the pyloric part by an angular depression in the lesser curvature - the incisura angularis. The cardiac portion of the stomach lies above this notch, the pyloric portion below. The fundus of the stomach is that part lying above the horizontal plane passing through the cardiac orifice, and in man in the upright position, it is usually occupied by gas. The pyloric portion of the stomach is again divisible into two parts, the pyloric vestibule and the pyloric canal. The latter is a tubular constriction about three c.m. in length (in man), easily detected in adults, but best marked in infants. The pyloric vestibule is the part lying between the incisura angularis and the pyloric canal.

The muscular coats of the stomach are three in number - an outer longitudinal layer, a middle circular layer, and an inner oblique layer. The longitudinal fibres are continuous with those of the oesophagus, but end almost wholly at the pylorus. The circular fibres form a uniform layer over the whole extent of the stomach, and are thickened at the pylorus to form a projecting ring. They are continuous with the circular fibres of the oesophagus, but are sharply marked off from the circular fibres of the duodenum by a distinct septum of connective tissue. The oblique fibres are found chiefly in the cardiac end of the stomach, where they form a thick uniform layer covering both surfaces, some passing from right to left and others from left to right round the cardiac end.

In the distended organ, the part of the stomach lying between the fundus and the incisura angularis has a tapering shape, narrowing from above downwards. When an animal is examined with the X-rays immediately after receiving a meal, a wave of constriction is seen to appear, after a short interval, near the beginning of the vestibule, and to move slowly towards the pylorus. This is soon followed by other similar waves regularly recurring in the same region. In a short time, faint constrictions appear near the middle of the body of the viscus and course towards the pylorus, growing deeper as they proceed. These gastric waves do not pass the pylorus into the duodenum, this fact probably being accounted for by the interruption of muscular continuity between stomach and duodenum by the septum of connective tissue already noted. In man, the rate of these waves is about three per minute (CANNON[94]). As digestion proceeds, changes occur in the shape of the stomach, These changes affect the pyloric portion only slightly - the first part to decrease in size is the part of the body of the stomach over which the waves are passing, and this part contracts into the form of a tube with the full cardiac pouch above, and the active pyloric portion below (CANNON[95]). Along this tube shallow peristaltic waves continue to pass, while the radiating fibres at the cardiac end gradually force the contents of the upper end of the stomach into the tube. Thence the food is passed onwards as fast as it is received, the peristaltic waves which press it forward becoming deeper and stronger as they approach the pyloric outlet. About an inch from the pyloric canal the wave becomes so marked that part of the vestibule becomes almost completely isolated from the rest of the stomach, and by contraction of its walls this part becomes smaller in every direction, forcing part of its contents through the pyloric opening, if patent, while the remainder escapes as an axial reflux stream back into the stomach. This process continues until the stomach is empty. The first clear description of gastric movements was given by Cannon in his reports of X-ray investigations in cats, and he showed later that similar changes occur in man; an observation which has been confirmed by Hertz and others.

Cannon concluded from his experiments that the two parts of the stomach have distinct functions. "The left half is a reservoir in which the food is not mixed with the gastric secretion, and from which the contents are slowly pressed out into the active right half. The pèristaltic waves coursing over the right half mix the food with the gastric juice, expose it to the mucosa of the vestibule for absorption and for the continuance of gastric secretion, churn the unbroken particles of food until they are triturated, and finally expel the chyme into the duodenum" (CANNON[96]).

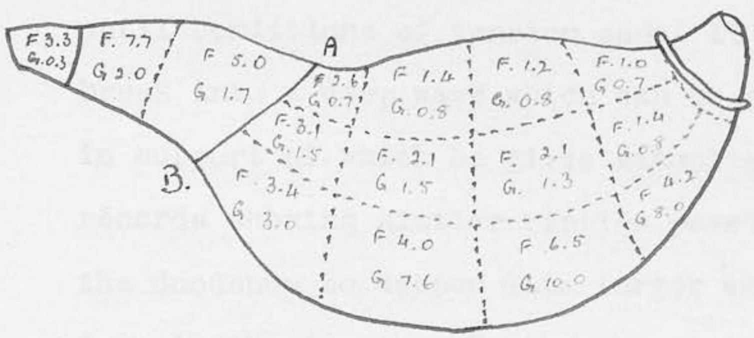
The question next arises as to the way in which these processes are initiated and regulated. Cannon has tied the digesting stomach at both ends, removed it from the body to a bath of warm oxygenated Ringer's solution, and introduced a glass tube rising above the gastric level; under which conditions he observed peristaltic waves passing over the organ for half an hour, during which time, also, the contents were gradually discharged as the volùme diminished (CANNON[97]). Both the peristaltic waves, therefore, and the tonic contraction of the left half of the stomach can occur independently of the central nervous system. Furthermore the peristaltic waves can occur independently of the local nervous mechanism as well. This was shown in an experiment by Cannon in which he cut rings through the muscular coats of the stomach to the submucous connective tissue, in this way entirely severing Auerbach's plexus. In one animal, in which six such rings were cut between the cardiac end of the stomach and the pylorus, after three weeks the waves were seen to pass with perfect regularity, much as in a normal stomach (CANNON[98]). The arrival of a wave at a junction stretched the muscle in the segment below, and this responded by contracting. The contraction passed downwards and not backwards again, presumably on account of a refractory phase in the neuromusculature above. It is probable that the co-ordination between the two parts of the stomach - the tonic contraction of the fundus above and the rhythmic contractions in the pyloric part below - depends on the local nerve plexus, but the peristaltic waves are myogenic (STARLING[99]). As in the case of the antiperistaltic waves in the colon, a wave is apt to appear at the spot where a certain balance is struck between the tone of the muscle, and the internal tension, (CANNON[100]). If the internal tension be too high in relation to the tone of a given segment, no contraction of the segment will occur; and similarly if the internal tension is too low.

In the conically shaped (full) stomach, however, there will be one point at which the relation of internal pressure and tonus of muscular wall are such that the neuromusculature responds by contraction. The material displaced by this contraction probably escapes into the cardiac region, where, as Cannon says, the weakest muscles are working against the greatest obstacles. As the contracted ring relaxes, however, it is stretched by the tonic pressure from the cardiac end, and a fresh contraction results. In this way is produced a pulsating ring, and each pulsation sends off a wave which travels towards the pylorus; the wave does not travel towards the cardia, because of the pressure conditions; the cardia sac is already subject to too great a pressure in relation to its tonus to be able to respond. Otherwise it would itself be the pulsating area.

According to Alvarez "local peculiarities in the muscle with graded differences in rhythmicity, irritability, tone and latent period probably have most to do with directing the peristaltic wave as it passes over the stomach. As in the heart, so here, the waves probably have their origin in the most highly rhythmic and sensitive area. We may say, perhaps, that the region on the lesser curvature next the cardia is the pacemaker for the stomach.

It must be rembered, however, that the activities of the heart and stomach are very different. In one, the impulse travels so rapidly that the organ appears to contract as a unit; in the other a series of waves travel slowly over the sac, gently kneading its contents" (ALVAREZ[101]). In support of this contention he points out that the muscle on the lesser curvature near the cardia is soft to the touch, like coagulated fibrin, while that in the pyloric vestibule has a different colour, and is tough like gizzard. Stimulation of strips cut from these areas gives entirely different contraction curves, and if they are put into warm oxygenated Locke's solution, two different types of rhythmic activity are seen. These differences in the muscle from these two areas conform to the different kinds of work required of them. The upper end of the stomach serves largely as a reservoir to hold the food, the lower as the mill to do the heavy work. To show the differences in rhythmicity, Alvarez cut strips of muscle from different parts of the stomach, and got them to contract in warm aerated Locke's solution. The segment from the lesser curvature near the cardia always showed the greatest tendency to rhythmic contraction. Strips from the greater curvature, and especially from the pyloric vestibule were slow in starting, and many would not contract at all. The rate varied ordinarily from about eleven at the cardia to about two near the pylorus (ALVAREZ[102]). He noted also that in the case of strips cut from the stomach near the cardia, the edges of the cut retracted, so that the piece was several times smaller than the hole; whereas in the case of strips cut from the larger curvature, the pieces sometimes stretched a little and became even larger than the hole. From these observations he infers that the muscle of the cardia shows more tone than that of the greater curvature. Differences in the amplitude of contraction in the different segments he ascribes partly to these differences in tone, and partly to differences in the structure and arrangement of the muscle fibres. He also describes a definite gradation in the ratio between the latent periods with faradic and galvanic currents in different parts of the stomach (Fig. 5).

He obtained similar results with strips of muscle taken from various parts of the small and large intestines, and in his view the essential factor in the propulsion of food along the alimentary canal is this gradient



Anterior surface of the stomach of the cat, showing the average intent periods after faradic and galvanic stimulation in different regions. The figures indicate seconds. A.B. is the dividing line between the pars pylorica and the body of the stomach. The other unbroken line represents the pylorus.

(The Mechanics of the Digestive Tract, Alvarez.) p.64.

of forces leading from the stomach downwards; a gradient depending on the structure and arrangement of the actual muscle fibres, and not dependent on any nervous mechanism. Cannon's observation that the gastric waves appear now here, now there on the greater curvature he explains as due to the fact that the wave has travelled as an unnoticed ripple from the "pacemaking region" in the cardia until conditions of tension cause it to break into a deep wave which can be seen: in support of which he gives examples of records showing similar ripples passing from the duodenum to deepen into larger waves lower down in the tract. Further he states that strong action currents run rhythmically even over stomachs that show absolutely no sign of peristalsis (ALVAREZ[103]).

Whether then, the gastric peristaltic waves start at one definite spot in the stomach wall, or at varying spots under different conditions of tension and pressure, it appears that they originate in the muscles themselves and are propagated from fibre to fibre without any actual assistance from the nerve plexuses being necessary. The wave in the stomach is not a true peristalsis, as it is not preceded by a wave of relaxation, and hence the intervention of nerve reflexes becomes unnecessary. Nevertheless, for the normal activity of the stomach, the normal tone of the gastric wall is all important, and this tone is normally maintained and regulated by nervous influences. Under normal conditions, the vagi have much to do with regulation of the muscular tone. Stimulation of the vagus may cause, under different circumstances, either contraction or relaxation of the gastric muscles, as both motor and inhibitory fibres are present in the nerve. The usual effect of such stimulation is a primary inhibition, followed later by increased tone and greater amplitude of the rhythmic waves (CANNON[104]). Section of both vagi causes abolition of the gastric movements for some days, but as time passes, a compensatory mechanism comes into play, the tone of the muscles is restored, and the gastric movements may return and present many of their normal characteristics, as both Pavlov and Cannon have proved. This fact, however, does not diminish the importance of vagus action in maintaining tone under normal conditions. It merely indicates that under certain abnormal conditions, the neuromuscular apparatus exhibits the power of compensatory re-establishment of more or less normal tone conditions. Repeated stimulation of the vagi causes an increased and more permanent tonic contraction of the gastric wall, and with this increase of tone there is also an increase of the peristaltic constrictions. Removal of the vagal influence results in a temporary paralysis, and the peristaltic movements, even when restored, are at first very shallow. The function of the vagus, therefore, seems to be that of keeping the gastric muscles at such a state of tension or tone that they are enabled to react properly to the stimulus of the gastric contents. We have already noted the effect of the vagus in producing a flow of gastric juice at the commencement of a meal, in response to a psychic stimulus, appetite. Cannon suggests that the impulses calling forth this juice are accompanied by others which produce a psychic tonus of the gastric muscles; (CANNON[105]) a state of affairs quite as necessary for proper digestion as is the gastric juice. The latter is useless unless it is incorporated with the food. This action of the vagus is suggested, also, by the observation, which has been repeatedly made, that a large draught of water taken to quench thirst may arrive in the duodenum almost at once. Water does not cause any psychic secretion of gastric juice, and its ingestion under these circumstances is evidently accompanied by a lack of tone in the pyloric muscles, as otherwise it would not escape so readily into the duodenum.

Once the appetite juice has been provided, it initiates a process by which fresh juice can be formed without assistance from the nervous side. So too with the gastric tone necessary for digestion. Once the peristaltic movements are started, section of the vagus, and even removal of the stomach from the body does not abolish them. Provision is evidently made for a continuance of the necessary tone by some local mechanism.

The inhibitory fibres in the vagus are employed in at least one important reflex whereby the entrance of food into a tonically contracted stomach is rendered easier. By the introduction of a balloon into the cardiac end of the stomach through an oesophagotomy opening, variations in the intragastric pressure and volume can be measured. Cannon and Lieb have shown by this means that the act of swallowing causes a fall almost to zero of the intragastric pressure; an automatic mechanism of obvious value in the introduction of a bolus into the stomach. If the vagi are cut, the phenomenon does not occur (CANNON[106]). The complaint of a feeling of fulness at the commencement of a meal, so commonly made by patients with atonic and toneless stomachs, may be connected in some way with this reflex. Obviously, if the tone of the stomach is low, and the muscles fully relaxed, the attempt of the vagus to relax them still more is doomed to failure.

The effects of the splanchnic nerves on stomach secretion and movements we have already noted. Stimulation of the sympathetic causes diminished tone and weakening of the rhythmic contractions. Extreme loss of tone and total cessation of peristalsis follow the injection of adrenalin. Some of the abnormal effects seen after section of the vagus may be due to unrestrained action of the sympathetic, and it is obvious that in the normal animal, the maintenance of a normal state of tone in the gastric muscles is effected by means of a mutual action and reaction of these two opposing influences. Conditions interfering with this harmonious interaction are calculated to lead to disturbances in the normal processes of digestion, which may well be reflected as symptoms of disease.

THE SENSIBILITY OF THE STOMACH.

The question of the sensibility of the stomach, is of course, intimately associated with that of the afferent nerves of the autonomic system: and as our knowledge of these latter is at present very limited, it is not surprising to find considerable difference of opinion on the subject of gastric sensibility. On the continent, Lennander has made extensive observations on the subject, and he affirms that no sensations of touch, pain, heat or cold arise in any viscus innervated only by the vagus and the sympathetic. (LENNANDER[107]). Even when the viscus shows acute inflammation, it cannot directly give rise to painful stimuli. The pain associated with conditions of visceral disease, he ascribes to disturbances of the serous membrane and subserous connective tissue of the abdominal wall. This parietal surface derives its nerve supply from the spinal nerves, and according to Lennander resembles the cornea in that stimulation of its surface, results always in pain. In diseased conditions of the viscera, it may be stimulated by friction, or by dragging of adhesions (LENNANDER[108]). Mackenzie, as a result of observations made in the course of operations in which no anaesthetic was used, agrees with these conclusions of Lennander (MACKENZIE[109]), and states that visceral pain arising from disease of the abdominal organs is not felt in the organ concerned, but is invariably 'referred' to the peripheral distribution of cerebrospinal nerves in the external body wall. "In the normal processes of life, a succession of stimuli is continually passing by the afferent nerves to the spinal cord, and continuously playing upon the efferent nerves that run to muscles, blood vessels, and so forth, maintaining what we call "tone" in muscles and blood vessels. These processes are conducted so that they give rise to no appreciable sensation. If, however, a morbid process in a viscus gives rise to an increased stimulus of the nerves passing from the viscus to the spinal cord, this increased stimulation affects neighbouring centres, and so stimulates sensory, motor, and other nerves that issue from this part of the cord. Such stimulation of a sensory nerve will result in the production of pain referred to the peripheral distribution of the nerve whose spinal centre is stimulated, so that the visceral pain is really a viscero-sensory reflex. If the increased stimulus affects a motor centre, then a contraction of the skeletal muscle results, and thus is produced the visceromotor reflex" (MACKENZIE[110]). As will be seen from this description, the viscero-sensory "reflex" is not a true reflex, as no motor nerve is concerned in the production of the phenomenon. Other observers, while admitting the occurrence of referred pain, describe also a somatic pain produced actually in the viscus concerned; and Hurst has explained the fact that the pain (e.g. of a gastric ulcer) is felt sometimes at a distance from the offending organ, by the Law of "average localisation" (HURST[111]), according to which the individual refers the pain to the place usually occupied by the diseased viscus; an explanation which Mackenzie describes as a "pure assumption which neglects or ignores the essential facts" (MACKENZIE[112]) it is evident, then, that important discrepancies exist among investigators, and the question of the localisation of gastric pain cannot yet be regarded as definitely settled. The afferent impulses, however, arising from the stomach are not of the same sensory type as those originating in skin and voluntary muscle, as the viscera are devoid of sensory nerve endings of the types found in skin and voluntary muscles. Clinical experience has shown definitely that the stomach can be cut, crushed or burned in the conscious subject without any production of pain. Hurst has shown experimentally that the stomach is insensitive to ordinary tactile stimuli (HURST[113]). He also states that the stomach is equally insensitive to heat and cold and that the sensation felt on drinking hot or cold fluids is to be ascribed to the lower end of the oesophagus, the sensory impulses being conveyed by the vagi. Previous experiments with the stomach tube which seemed to credit the stomach with some power of discrimination between heat and cold he explains as being due to warming or cooling of the tube by the liquid, and he states that if a double tube is used, it can invariably be shown that the stomach is absolutely insensitive to thermal stimuli. In the majority of cases, this, no doubt, is quite correct; but there do seem to be some instances in which there is some sensibility of the stomach to heat and cold. Recently while washing out a dilated stomach on a very cold night I used cold water for the final wash. The patient subsequently volunteered the statement "That felt cold right down to there", placing her hand at the same time not over the sternum, but over the left iliac region. I repeated the process on several later occaions, and always with the same result. Furthermore in this lady, the cold water invariably sets up brisk retching movements, and instead of the normal quiet return seen with warm water, the liquid is ejected with considerable force. It is evident that in this particular patient, at all events, the cold water sets up nerve impulses resulting in reflex contractions of the abdominal muscles; and it is difficult to reconcile the sensation of cold in the iliac region with the view that the sensory stimulus arises in the oesophagus.

In a case of severe bulbar paralysis, in which there were no sensory or motor disturbances present in the limbs or trunk, Hurst found that hot or cold fluids introduced into the oesophagus produced no sensation. He infers, therefore, that thermal sensations in the oesophagus are conveyed to the central nervous system by the vagi, and not by sympathetic fibres (HURST[114]).

For long it has been believed that the painful stimuli arising in the stomach in cases of gastric ulcer were due to the effect of the acid gastric juice on the nerve endings exposed in the ulcer. By introducing 0.5 per cent of hydrochloric acid into the empty and ulcerated stomach, however, (the diagnosis being confirmed in six cases by subsequent operations), Hurst showed that this view is erroneous. The acid caused no sensation whatever (HURST[115]). This does not mean that the acid does not set up nerve impulses -it merely proves that it does not in itself originate painful nerve impulses. That the acid has something to do with the pain in such cases is obvious from the fact that administration of alkalies gives such speedy relief. Hurst explains the pain in hyper-acidity by assuming that such acidity gives rise to an increased number of afferent impulses from the stomach to the cord. These impulses are not in themselves of a painful nature, but they give rise to reflex peristaltic movements which may be painful (HURST[116]). He assumes that the acid has a greater power of stimulation on the nerve endings exposed in an ulcer, and points out, also, that the exposed nerve fibres in the deeper parts of the stomach wall are more numerous than those in the mucous membrane. Hence arises an increased number of nerve impulses passing from the stomach to the cord and back again, an increased fluctuation, causing in the case of a gastric ulcer, increased peristalsis, and in the case of a duodenal ulcer, inhibition of the relaxation of the pylorus. This view, as Hurst states "is confirmed by the speedy relief given in the pain of gastric ulcer by paralysing the afferent nerve endings in the ulcer by means of orthoform."

Afferent stimuli originating in the stomach can be demonstrated by the direct introduction of chemical substances such as alcohol and carminatives. Strong alcoholic solutions induce a feeling of warmth, which does not appear immediately, but after a latent period of a minute or two. Miller's experiments with mustard on the mucous membrane of the stomach have already been referred to, and they demonstrated the production of afferent impulses conveyed centralwards by the vagi, (MILLER[34]). Ducceschi has also presented evidence that stimuli applied to the gastric wall by thermal, mechanical or chemical agencies are capable of originating afferent impulses, demonstrated by reflex changes in the rhythm and frequency of respiration (DUCCESCHI[117]). The feelings of satiety and comfort after a meal are probably produced in part through afferent impulses from the stomach by way of the vagi (LOEB[118]), and Hurst believes that the "illdefined sensations which occur in all parts of the alimentary canal and which may be grouped together as the 'sensation of fulness" are due to stretching of its muscular coat, and constitute a form of muscle sense, which is probably shared by all hollow viscera" (HURST[119]).

Another sensation connected with the stomach is that of hunger, in the study of which Cannon and Washburn performed some interesting experiments. The latter accustomed himself to the presence of a balloon in the stomach, connected with a recording lever. The writing point of the latter being concealed from him, he indicated by means of a second lever the occurrence of individual hunger 'pangs', and was able to demonstrate in this way that the unpleasant sensation concerned was due to muscular contraction of the wall of the stomach (CANNON[120]). Periodic contractions of the stomach walls in fasting animals had been noted by several observers, including Pavlov. The latter observed also that these movements could be inhibited in a purely psychic manner, by the mere exhibition of food to the hungry animal or by sham feeding (PAVLOV[121]). The instantaneous arrest of the movements which occurs at the sight of food is probably brought about by means of inhibitory fibres in the vagi, with the obvious purpose of allowing the food, when ingested, to remain in the stomach. A similar inhibitory action of the vagus is suggested, also, by Cannon's observation that the unpleasant sensation of hunger can be momentarily abolished by the act of swallowing (CANNON[122]). The actual contractions of the fasting stomach are not abolished by section of the vagi, and do not therefore depend on any efferent impulses from the cranial autonomic nerves. Evidence has been adduced that the hunger contractions may be due to some substance circulating in the blood, as the injection into a normal animal of blood from a fasting animal can induce spasm or tetanus of the gastric muscle - an effect which is absent when the blood of a well-fed animal is injected (CANNON[123]). The actual sensation of hunger, then, appears to be due to afferent impulses arising in the stomach walls from stimuli originated by contraction of its muscular elements.

Bennett and Venables, as a result of experiments on the effect of emotion on gastric secretion and motility, conclude that the reverse of this occurs, and that "when the brain is filled with the conception of hunger, vigorous gastric peristalsis is the result" (BENNETT and VENABLES[124]). "There is, however, nothing contradictory in these results; what could be more logical than that so complicated a reflex should be reversible? The timid traveller sees a robber behind every bush" (BENNETT and VENABLES, Loc cit.)

We may conclude, then, that the ordinary forms of stimuli, which, when applied to the sensory nerve-endings of skin and voluntary muscle produce sensations in consciousness, do not give rise to appreciable sensations when applied to the mucous membrane of the stomach. The stomach is "insensitive" to the ordinary stimuli which affect the surface of the body. Nevertheless, such stimuli are probably capable of originating afferent impulses which do not normally arrive at the level of consciousness, but which manifest themselves by various reflex. modifications of respiration, pulse rate, etc. Certain chemical substances may apparently give rise to afferent impulses from the gastric mucosa resulting in a sensation of warmth, but the actual sensory nerve endings concerned in this stimulation are not definitely known. The stomach is capable, however, of producing definite sensation, probably from stimulation of sensory nerve endings in the muscular coats, the stimulus originating in the contraction of the muscular fibres. The cramplike pain of gastric ulcer and hyperacidity, and the pangs of hunger, are probably produced in this way. The separate sensation of fulness and distension may be caused by stimulation of similar sensory nerve endings in the muscular coats from stretching of the latter. It seems highly probable that the spinal cord contains reflex centres, to and from which afferent and efferent impulses are constantly passing. While the nature of the afferent impulses (and of many of the stimuli originating them) is not definitely known, many of the efferent impulses are probably motor and secretory, and must cause modifications in the contraction of the gastric muscles, and in the secretion of the digestive juices and mucus.

CONDITIONS WHICH LEAD TO FUNCTIONAL DISTURBANCES OF THE STOMACH.

1. Abnormal states of the nerves.

Under ordinary circumstances, the normal functions of digestion are carried on quietly and unobtrusively by the organs concerned, and the responsibility for the efficient working of the process rests with the involuntary nervous system. The latter, however, is by no means independent, as is quickly apparent when anything goes wrong. The connections between the sympathetic and the central nervous system have already been examined, and it seems probable that under ordinary circumstances, impulses pass regularly from the viscera to the brain. The sensations of fulness and distension, and of hunger, evidently depend on such impulses. Slight departure from the normal course of events in digestion are readily appreciated in consciousness, and in one large class of nervous dyspeptics, even the gastrointestinal movements appear to give rise to stimuli which reach the level of consciousness. "After listening to the tales of hundreds of neurasthenics it would almost seem as if their viscera had become as sensitive as their skins; they can apparently feel their brains working, their hearts beating, and their alimentary canals doing the work of digestion" (REYNOLDS[124a.]). Frequently also in normal individuals, the nightmare consequent on an indigestible supper may be the only evidence of digestive derangement, and this can be readily explained on the hypothesis of increased number and intensity of the stimuli passing into the central nervous system from the alimentary tract - an increase in the fluctuation normally going on.

The presence in the spinal cord of reflex centres, to and from which afferent and efferent impulses are constantly passing, has already been noted. Normally these impulses pass backward and forward without causing any disturbance in neighbouring centres, but should they become unduly intensified, adjacent portions of the cord are apt to become irritable. Sensory nerves affected in this way result in afferent impulses to the brain which are interpreted by the latter as painful stimuli from the area of distribution of the nerve fibres involved; while irritation of efferent nerves leads to contraction of the muscular elements which they innervate. As the cells and fibres in closest proximity to the reflex centres of the cord are the first to be affected by undue activity in the latter, the disturbances which result are reflected fairly constantly along certain paths. Sensory symptoms due to stomach disorders are usually referred to the epigastrium, (MACKENZIE[125]) in the sensory area of the sixth and seventh thoracic nerves; and the visceromotor reflex shows itself first in the upper portion of the left rectus muscle, which derives its nerve supply from the sixth thoracic nerve. Pain from gastric affections is also frequently referred to the back below the shoulder blades, especially the left. Frequently the pain is associated with hyperalgesia of the skin and deeper structures, the hyperalgesic area being usually situated in the epigastrium. The area affected is not sharply defined, the borders being very indefinite; and it frequently extends in the form of an irregular band round the left side.

Hyperalgesia of the skin is always accompanied by an increase in the superficial reflexes, as might be expected. The response obtained from slight stimulation of the skin is exaggerated, and the area of skin from which it may be obtained is considerably increased. "The extension of this area follows some peculiar law, as responses cannot be obtained from the whole of the left chest, but only from an area extending in an irregularly shaped band up the side to the axilla", (MACKENZIE[126]).

It is doubtful whether a definite hyperalgesia with its associated increased cutaneous and muscular reflexes ever occurs apart from an organic lesion. Pain in functional disease of the stomach is usually referred by the patient to the left of the epigastrium or left hypochondrium, or to the back between the shoulder blades. Very rarely is it localised to a small area, and very rarely, if ever, is it accompanied by the hyperalgesia of the skin so common in organic disease. The reason for this is not quite clear, but probably the disturbance of the afferent impulses from the viscera is of too diffuse a nature, in the case of functional disease, to produce the necessary hypersensitive spots in the cord. In organic lesions, the diseased area supplies a more or less continuous stream of impulses which impinge on the cord over a certain localised area, while in functional dyspepsia the trouble is more wide-spread and the abnormal afferent impulses to the cord are not focussed on any one particular part. Nevertheless, the pain in the back, commonly present in cases with no organic lesion, is a referred pain, produced in much the same way as the hyperalgesia of the skin, yet never associated with the latter.

Another point about this induced irritability of spinal cord centres, is, according to Mackenzie, the fact that pain is the only resulting sensation. Abnormal afferent stimuli from the viscera do not produce a feeling of cold or any sensation but that of pain (MACKENZIE[127]) Mackenzie explains this by suggesting that for any other sensation than pain, a special receptor organ is necessary; an explanation which does not seem wholly satisfactory. I have, indeed, seen one case in which a sensation of cold was produced repeatedly from cardiac disease. The associated pain and hyperasthesia was of the usual type, occupying the left side of the chest and radiating down the left arm. In addition to this pain, however, the patient complained bitterly of a feeling of intense cold in the mouth and throat, involving even the teeth, and extending downwards in the middle line of the body to the lower end of the sternum. This patient has been confined to bed for the past six months, but still has occasional exacerbations of pain, which are still accompanied by the feeling of intense cold in the area described.

In addition to these referred sensory disorders, there may be a true visceral gastric pain, resulting probably from excessive stimulation of the afferent nerves. The nervous channels used in this production of pain are probably those which normally convey afferent but unfelt impulses to the cord, the natural function of such impulses being the production of reflexes. It is improbable that the viscera are supplied with nerve fibres having no other function than that of conveying painful stimuli, since such pain fibres may not be required once in several generations. It is a disturbance in normal reflex processes that gives rise to visceral pain, and the adequate stimulus necessary is apparently distension of the muscular coat. In the case of the stomabh, distension of one part of the organ is more commonly the cause of pain than distension of the whole organ (HURST[128]). The production of such partial distension depends on some disturbance of the reflex nerve processes already noted as controlling and regulating the activities of the stomach. Abnormally strong peristaltic waves will increase the pressure in the pyloric part of the stomach; they also offer more resistance to the axial reflux stream of chyme from the small pyloric chamber cut off by the peristaltic contraction from the remainder of the organ, and as a result the internal pressure in this chamber is increased to a point where the tension on the muscular walls causes pain. Any factor which tends to prevent relaxation of the pylorus on the arrival of a peristaltic wave, will also tend to cause an increase of pressure in the pyloric part of the stomach and so lead to sensations of pain. The activities of the pylorus are controlled, as we have seen, by a local reflex mechanism, which operates from both the gastric and the duodenal side of the sphincter. Acid in the duodenum has a powerful effect in closing the pylorus, as also has the presence of anything in the stomach which might injure the duodenum. Hard particles of food in the stomach, from inefficient mastication, or improper diet, give rise to increased peristalsis and at the same time cause the pylorus to remain tightly closed. This leads to increased pressure in the pyloric end of the stomach, tension on the muscle fibres, and pain. In the same way, excess of acid leads to pain by stimulating peristalsis, and by reflexly closing the pylorus from the duodenal side. Actual spasm of the gastric muscles may, under some conditions, provide an adequate stimulus of sufficient intensity to cause pain.

A second very common complaint in "indigestion" is that of flatulence. In cases of gross pyloric obstruction, such flatulence may be due to actual fermentation in the stomach, but in functional dyspepsia, fermentation in the stomach is very rarely responsible for sufficient gas to cause symptoms, and the trouble seems to be rather a disturbance of those normal reflex processes by which the vagi adjust the tone of the stomach muscles to the volume of ingested material. X-ray observations frequently show in a toneless and dilated stomach, considerable quantities of gas, while the patient may complain of no sensation of flatulence at all; whereas on the other hand, a small amount of gas in a very hypertonic stomach may be accompanied by extreme discomfort. The amount of discomfort seems to vary, therefore, according to the tension exerted by the walls of the stomach, on the contents of the viscus. In the dilated stomach though the presence of a considerable amount of air may be unassociated with any sensation of fulness, nevertheless the introduction of food will cause such a sensation. This must be due to the increased dilatation of the stomach produced by impulses through the vagi as each bolus of food enters the stomach. The increased dilatation is accompanied by increased tension, and hence the feeling of fulness. As Hurst points out, therefore, a sensation of fulness in the stomach may result from two diametrically different conditions - excessive and deficient gastric tone (HURST[129]). This sensation of fulness, whether due to the presence of air or not, is usually described by the patient as "flatulence". In some cases, also, an irritable spasm of the cardiac orifice is misinterpreted by the patient as gas in the stomach, and he attempts to relieve the condition by belching. In the process he swallows bolus after bolus of air until the pressure in the stomach is sufficient to force the cardiac sphincter, and the air is expelled with some force and considerable relief, and the process recommenced once more. Other cases occur in which a sense of extreme flatulence is complained of, but which passes off without the expulsion of any gas. Such cases may be due to a reflex spasm of the diaphragm leading to increased intra-abdominal pressure.

Kelling (KELLING[130]) has demonstrated the presence of a reflex mechanism by means of which the tone of the muscles of the abdominal wall is adapted to the varying volume of the contents of the alimentary canal. Such a mechanism is necessary to prevent an undue rise in the intra-abdominal and intragastric pressure on the consumption of a meal, but Hurst denies that the feeling of fulness which follows a heavy meal is due to any stretching of the abdominal wall. The following case, however, seems to indicate that in some instances, a complaint of distension may be due to some failure of this normal regulating process.

C.P. Male, aet 33. Complains of flatulence and distension after meals, and "swelling of the abdomen". He has always had a somewhat prominent abdomen, which has been more marked during the past two years. X-rayed while in the Army, and told that he had a "very large colon". He states that at present a meal, unless of small bulk and eaten extremely slowly always causes a feeling of tremendous distension, increasing with the amount eaten, and obliging him to loosen all his clothes, which affords slight relief. Measurement during quiet respiration, at the level of the umbilicus and immediately after his midday meal (when he was complaining of extreme discomfort) showed a girth of 31-32 inches. Measurement five hours later, when the feeling of distension had passed off, showed 31¾-32¾ inches.

Thus the feeling of distension in this case was greatest when the girth measurement was least, and it seems possible that the normal regulating mechanism which Kelling describes, had somehow failed to act as efficiently as usual.

The actual sensation of flatulence - the conscious feeling of distension of the internal organs, is probably produced by afferent impulses proceeding to the brain from the viscera; impulses which probably originate from an adequate stimulus applied to some peripheral sense organ in the wall of the viscus concerned. This adequate stimulus seems to depend on stretching of the muscular elements of the wall under certain conditions of tone, but the exact method of its production is unknown. The main function of a sense organ or "receptor" is, as Sherrington says, to lower the threshold of excitability of the reflex arc for one kind of stimulus, and to heighten it for all others (SHERRINGTON[131]). The receptor organs with which we are familiar in the skin may, under some circumstances, become hypersensitive. The application of a mustard plaster to the skin, for instance, makes the patch of skin concerned much more sensitive to thermal stimuli than surrounding areas, and this may be attributed to a lowering still further of the threshold of excitability of the nervous arcs concerned, by irritation of the receptor organs. Such variations in the activity of the receptors may account for the common complaint of flatulence in some cases of nervous dyspepsia. There is an increased perception of the stimulus. But in the case of the sensation of fulness or flatulence the stimulus itself depends, for its production, on certain conditions of tone in the gastric muscles, and this tone, as we have seen, is constantly being modified by reflex processes through the vagi and sympathetic nerves. Excess of tone may be produced through excessive vagus action, as in the cases of cardiac spasm previously mentioned. It is well known, also, that smooth muscle, when removed from all nervous connections, is apt to undergo considerable increase in tone. Thus Cannon found that after section of the extrinsic nerves, the stomach of the cat may contract to a hard narrow tube of $1\frac{1}{2}$ to 2 centimetres in diameter (CANNON[132]) and it may be that the condition of increased tone present in so many cases of flatulent dyspepsia may sometimes depend not on an excess of nervous stimulation, but on a lack of it. The present state of our knowledge does not permit us to follow out in detail the exact nervous processes involved in the production of the adequate stimulus for the sensation of fulness or flatulence.

The presence of air or gas in the stomach may have the effect of keeping the acid contents of the viscus away from the stomach wall in the region of the cardia, and so interfere with one of the reflexes concerned in keeping the cardiac orifice closed. Regurgitation of gas and fluid may occur from this cause. Failure of this nerve reflex also accounts, probably, for some cases of furred tongue associated with foul breath and an unpleasant taste in the mouth, and frequently a constant sensation of nausea; effects which can all be explained by deficient locking of the cardiac entrance.

In many cases of functional dyspepsia, the complaint is merely one of discomfort after meals - a feeling of weight and fulness in the epigastrium, and many authors describe a condition of gastric hyperaesthesia to explain these cases. The condition is regarded as a supersensitiveness of the nerve endings in the mucous membrane of the stomach or in the subperitoneal tissue (MACLENNAN[133]), as a result of which the patient becomes conscious of the digestive processes, and the mere contact of food with the mucous membrane of the stomach gives rise to discomfort or pain. Mere supersensitiveness of these nerve endings, however, is not sufficient to explain this symptom. Even in normal individuals as we have seen, these nerves conduct afferent impulses to the brain and cord, but such impulses do not affect consciousness. They result in reflexes affecting the motility and secretion of the gastrointestinal tract, the rhythm of the heart and respiration, etc. The feeling of weight indicates a disturbance of the normal reflex paths taken by the impulses, in virtue of which they arrive at levels of the central nervous system from which, normally, they are excluded. The increased number of such stimuli, however, passing into the central nervous system may produce a corresponding supersensitiveness of adjoining centres, and in this way the barriers excluding visceral impulses from the levels of consciousness may be broken down, and the impulses allowed through. The afferent stimuli also may lead to exaggerated peristalsis and increased tension and in this way give rise to a feeling of discomfort or pain through the medium of the sensory nerves of the muscular and subperitoneal connective tissue layers.

Allied to this condition is that of gastralgia, which is usually regarded as a neuralgia of the gastric terminations of the vagus nerve. Maclennan describes four varieties of gastralgia, according to the cause (MACLENNAN[134]) (1) A toxic form, due to indiscretions in diet, abuse of alcohol, tobacco, etc., (2) A severe form occurring in organic disease of the central nervous system - tabes, myelitis (3) A form occurring in functional derangements of the nervous system - hysteria, neurasthenia, (4) Reflex gastralgia occurring from disease of the abdominal or pelvic viscera. Disease of the sympathetic ganglia has also been adduced as a causal factor in the production of gastralgia. The characteristic feature of this affection is that the onset bears no relation to the taking of food. The attacks are usually separated by intervals of complete freedom from pain. The individual attack begins suddenly and may be slight, or on the other hand, very severe. The mere intensity of the pain, in fact, may occasion a fatal result (ALLBUTT[135]). A comparatively rare manifestation of functional disorder of the stomach is an abnormal craving for food, with an insatiable appetite - bulimia. Many theories have been advanced to account for the condition. Excessive contraction of the gastric muscle, from the presence of some circulating toxin; anaesthesia of the endings of the peripheral nerves in the stomach, and irritation of the hunger centre in the medulla have all been quoted as causes of the symptoms. It is more likely, however, that the condition is due to some central change. Maclennan quotes a case in which, from time to time, attacks of extreme bulimia occurred in a patient suffering from acromegaly (MACLENNAN[136]).

It seems probable that in addition to these sensory disturbances, irritability of the gastric nerves will lead also to alterations in the secretions and motility of the stomach. In many cases, indeed, these occur along with the sensory disturbances. Thus the pain produced by unchewed lumps of food is due to the increased peristalsis and pyloric spasm induced thereby. The effect of unsuitable food in the production of vomiting is also well known. In the case of the gastric juice, however, the regulating mechanism is largely a chemical one, mediated by the blood stream. It has been shown that the first portion of juice is provided by a reflex mechanism, the afferent side of which does not lie in the stomach, and provision is made for a continuance of the secretion by means of chemical stimuli, independent of any nerve action. It is, however, possible to find a simple hyperchlorhydria due to over action of the vagus. In such cases we may find a stomach which shows no delay in emptying, and yet which yields a test meal of more than normal acidity. Cases also occur commonly of deficient action of the vagus, in which the gastric juice is diminished in amount, or absent altogether.

It has been shown also that mere interference with the normal peristaltic activities of the stomach will lead to variations in the secretions of that viscus from purely physical causes. Bennet and Venables formulate the law that "in a stomach which is secreting hydrochloric acid, any increase in the rapidity of emptying will by itself determine an increase in the acidity of the contents" (BENNET AND VENABLES[137]). They compare the stomach, in this respect, to a vessel with two taps - the pylorus representing the outflow, and the gastric glands the inflow. Turning on the pyloric tap, which tends to empty the organ, is compensated by an increased flow of juice from the glands. Thus an irritability of the gastric nerves leading to increased peristalsis and rapid emptying, will be accompanied also by secretory disorders, due to the resulting physical conditions.

An interesting hypothesis has been put forward by Eppinger and Hess as to the part played by abnormal states of the nerves in the production of visceral disorders. They imagine a condition in which one or other division of the Autonomic system is unduly irritable (EPPINGER and HESS[137]), and illustrate their hypothesis by means of the effects of drugs on the two divisions. Undue irritability of the cranial autonomic fibres (vagotonia),

is indicated by an abnormal response to injection of small doses of pilocarpine. A normal individual is scarcely affected by a small subcutaneous injection of this drug; whereas a vagotonic person is said to give a marked response, the hypersensitivity of his cranial autonomic fibres being manifest by narrowing of the pupil, profuse salivation, dyspnoea or spasm of the bronchioles, slowing of the pulse, increased secretion of gastric juice, tenesmus or vesical crises.
A sympatheticotonic, on the other hand, responds abnormally to small subcutaneous injections of adrenaline by dilatation of the pupil, dryness of the mouth, tachycardia, polyuria and glycosuria.

Clinically, cases of sympatheticotonia are said to show particularly vasomotor symptoms - emotional erythemas, flushing of the abdominal skin on slight stimulation, secretory disorders, disturbances of cardiac rhythm, respiratory troubles, constipation and various sensory symptoms, and various general symptoms affecting the metabolism, muscular tone, and the general nervous system.

In vagotonia, asthma and similar troubles, bradycardia, increased tone of gastrointestinal muscles, hyperchlorhydria, low blood pressure, eosinophilia, salivation and a high sugar tolerance, spasm and colic of the biliary passages are all described as part of the symptom complex.

If these two types could be distinctly recognised, and cases of vagotonia and sympatheticotonia identified by their reaction to the drugs indicated, there is no doubt that an important advance in the study of visceral neuroses would have been made. There are many objections to the theory, however, and Langdon Brown has emphasised many points in which the conception of Eppinger and Hess runs counter to established facts of physiology and pathology (LANGDON BROWN[139]). The conception is an interesting one which probably contains a germ of truth, but it will probably require considerable modification, and in its present condition must be regarded as 'not proven'.

It appears, nevertheless, that many of the common symptoms of functional dyspepsia may be due to disorder of the nerves controlling and regulating the activities of the stomach. Very many of these patients describe their troubles as the direct result of a preceding acute gastritis, and it seems probable that a nervous instability of this part of the nervous system may be originated in this way. A second very common and important accompaniment of dyspepsia is the presence of some septic condition in the mouth, nose or throat. Pyorrhoea and accumulations of tartar on the teeth are particularly common, and their causal relation to the dyspepsia complained of is easily demonstrated. It is of course possible that in these cases the organisms swallowed may cause a mild degree of gastritis which serves to keep up the irritation, but the evidence of inflammation is very slight, and the main factor concerned in the production of symptoms is the irritability of the nerves. In some cases, though rarely, there seems to be a particular idiosyncrasy on the part of the patient to particular articles of diet - a species of anaphylactic reaction. I have known a patient in whom the drinking of cow's milk invariably resulted in an attack of acute indigestion, terminating in vomiting. In a second case of this type, a woman aged 39, the eating of pork is always followed by a severe attack of acute indigestion, which always ends in the rejection of the offending food from the stomach. On the last occasion on which this patient ate pork (some six months ago), she suffered much more severely than usual, and continued to vomit, at intervals, for ten hours. The other members of the household, who all has the same food, were unaffected.

Since this occasion this patient's digestion (previously very good except for this one idiosyncrasy) has been somewhat impaired. This condition, however, is a rare one, and not of much practical moment. Far more important are conditions of undernutrition, anaemia and toxemia, all of which are of constant occurrence, and equally potent in the production of a general irritability of the nervous system which often seems to be specially apparent in the gastric nerves. The influence of toxemia is well shown in the case of pulmonary tuberculosis, in which it is not uncommon to find symptoms of gastric disorder before any disease in the lung is manifest or even suspected; a fact which indicates the importance of a thorough general examination of the patient in all cases of functional dyspepsia. The influence of toxic states on the gastric functions is also illustrated in the case of sprue. The aetiology of this disease has long been in dispute, but Scott has recently brought forward evidence that an essential factor in its production is an overburdening of the parathyreoid detoxicating functions, with a a resultant disorganisation of the calcium regulating functions of this gland (SCOTT[140]). Comparison of the calcium content in normal blood, and in that taken from cases of sprue showed that while the total calcium content of the latter may be only slightly diminished, the free calcium was always considerably below normal. By the administration of parathyreoid extract and calcium salts, Scott obtained an immediate and progressive amerlioration in the gastric and general symptoms of sprue, and this improvement was accompanied by a steady rise in the ionic calcium of the blood to the normal figure. When this was reached, the patients were well, and able to eat and digest an ordinary diet (SCOTT, Loc cit).

In many cardio-vascular diseases there are also usually marked gastric symptoms, produced probably in part through defective blood supply to the muscles and glands, in part through irritability of the nerves concerned. The cause of the dyspepsia in these conditions, however, is usually obvious.

2. Abnormal States of the Central Nervous System.

Gastric digestion may be deranged by abnormal states of the gastric nerves. It may also be affected by abnormal states of the central nervous system. It is a reasonable assumption that normal afferent impulses passing from the viscera to a hyperexcitable central nervous system may result in spreading of the impulse with the production of abnormally powerful or widespread efferent impulses. Disturbances of normal reflex processes are thus produced which are recognised clinically as symptoms. In many cases of true nervous dyspepsia, examination of the tendon reflexes will show them to be markedly exaggerated. The jerk obtained is much more active than normal, though the afferent impulses concerned (the strength of the stimulus) may be weak. Thus a normal afferent impulse proceeding to an abnormally excitable central nervous system results in a abnormally powerful response. It is reasonable to infer that similar results may follow on normal afferent impulses passing to the cord from the viscera, and the symptoms produced depend upon the end results of the reflex processes concerned. Alterations in secretion and motility, peristaltic unrest, vomiting, and similar symptoms may be produced in this way.

Other abnormal states of the central nervous system may have marked effects on digestion. It has been shown that in the normal process of digestion, the first portion of gastric juice secreted is produced through the stimulation of secretory nerves running in the vagi. These nerves are thrown into activity by a psychic state, appetite, or the desire for food, which in turn is produced through stimulation of the nerves of special sense - sight, hearing, taste and smell. This is an example of a highly complicated reflex act: complicated because the higher levels of the brain are called into play for its successful accomplishment. The reflex production of gastric juice by the mere exhibition of food to the hungry animal is a conditioned reflex; the nerve impulses concerned must pass through the higher cortical centres, where they are subject to various forms of control and inhibition, where they may be modified by volition and desire, and where, indeed, they may be extinguished altogether. Exactly how the cerebrum exerts this control over reflexes is an unsolved problem in physiology; a problem the solution of which would shed a flood of light on many diseases of the nervous system, but one which hitherto has baffled all inquiry.

One indispensible condition for the production of gastric juice in the experiment quoted is that the animal must show eagerness for food. Every other condition may be fulfilled, but if the dog be indifferent to the food (if, that is, he does not exhibit appetite), there will be no gastric juice. Appetite, as Pavlov says, spells gastric juice; and conversely, lack of appetite indicates lack of gastric juice. The commencement of gastric digestion depends, therefore, on a conditioned reflex process. Once digestion is started, the splitting up of the food substances gives rise to chemical bodies which are able, in turn, to stimulate the peptic glands to further activity. It is by this means that the process is continued, as naturally the reflex production of gastric juice is of considerably shorter duration than the process of digestion; but to set the mechanism in motion, the appetite juice is indispensible, particularly in the case of foods which exert only a feeble stimulus from the chemical side. The nervous control of the gastric glands is exerted not only through the vagus, but also through sympathetic nerves. These two sets of fibres, in the stomach, as elsewhere, are opposed in their functions. The vagus stimulates while the sympathetic inhibits the action of the gastric glands. Wertheimer demonstrated many years ago that strong stimulation of a sensory nerve in an anaesthetised animal quickly abolished any signs of activity in the stomach (WERTHEIMER[141]), and ten years before this Netschaiev, in Pavlov's laboratory, had shown that stimulation of the sciatic nerve for two or three minutes was able to inhibit the secretion of gastric juice for several hours (PAVLOV[142]). These results are explained as reflex inhibition of the stomach by way of the sympathetic nerves.

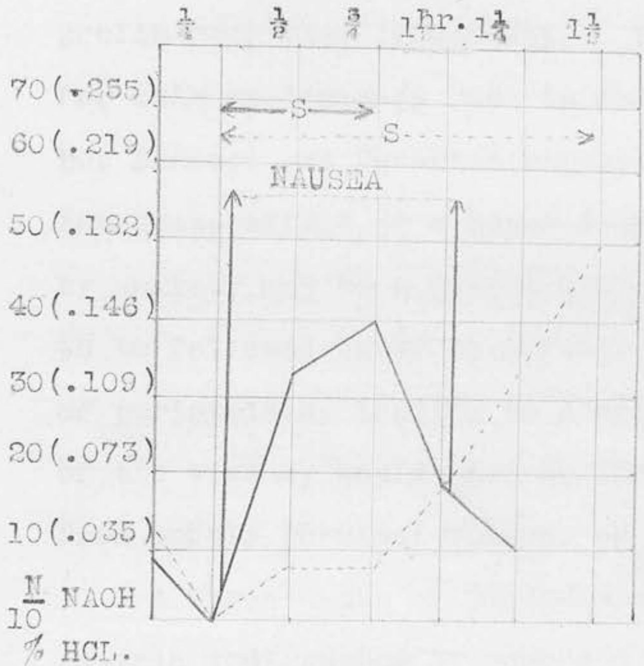
Sherrington in his study of the nervous system has shown that in the case of the skeletal muscles, stimulation of a flexor muscle is associated with simultaneous inhibition of its antagonist. This is due to a "reciprocal innervation" of the opposed muscles, and depends on an internal organisation of the central nervous system (SHERRINGTON[143]). The disturbances which can be produced by means of poisons such as chloroform and strychnine, upon reflexes affecting such opposed muscles, have already been noted.

Furthermore there are, as we have seen, peripheral oppositions in the viscera corresponding to the opposition between flexor and extensor muscles of the limbs, and as Cannon says "in all probability these opposed innervations of the viscera have counterparts in the organisation of neurones in the central nervous system - - - even though the sympathetic supply to the eye is severed, and is therefore incapable of causing dilatation of the pupil, nevertheless the pupil dilates in a paroxysm of anger - due, no doubt, because the response is too rapid to be mediated by the bloodstream, to central inhibition of the cranial nerve supply to constrictor muscles, i.e. an inhibition of the muscle which naturally opposes the dilator action of the sympathetic" (CANNON[144]). It is at least possible that there is a similar arrangement in the central nervous system for the orderly working of the neurones dealing with the digestive apparatus. As Cannon has shown, pain, the major emotions, fear and rage, as well as intense excitement, cause an instant inhibition of digestive activity by means of impulses conducted outwards by the splanchnic nerves. Such impulses are probably accompanied by an active inhibition of their opposing neurones.

Bennett and Venables have demonstrated in an original manner the effect of the emotions on gastric secretion and motility in the human subject (BENNETT and VENABLES[145]).

Their subjects were healthy young adults, who were accustomed to the presence of a Reyfuss tube in the stomach. After a small test breakfast of gruel, the subjects were lightly hypnotised, and in this state, various emotions were suggested to them, and the effects on the secretions noted by withdrawal of a small quantity from time to time. The effect of a suggested feeling of nausea on the secretion of HCL, is indicated in the accompanying figure taken from their article. It will be seen that the usual sharp rise in acidity is completely inhibited, and only at the conclusion of hypnosis does it rise appreciably, but it then rises more rapidly than normally. The alteration in the emptying rate is equally marked in this experiment. The specimen withdrawn at the end of hypnosis contained a large proportion of gruel, although in this subject the stomach was usually empty at this time. As the authors observe, the effect is probably an example of pure sympathetic inhibition, the pyloric sphincter being tightly closed, and the secretion of HCL checked by the emotion.

The effect of a suggested feeling of hunger was shown to be a marked increase in the



Effect of Suggested Nausea on gastric acidity and motility. Free HCL. only plotted. Continuous line = normal curve. Broken line ≡ experimental curve.

Rate of emptying shown ←S→

BENNETT and VENABLES.

secretion of HCL. Anxiety showed a strong sympathetic inhibition, with a noticeable delay in the rate of emptying, but a preliminary rise in acidity. The reason for this preliminary rise is not quite clear, but Bennett and Venables suggest that the immediate effect of a hyperadrenalism caused by anxiety may be a quickening of peristalsis, to be followed later by arrest. This quickening of peristalsis, leading to a more rapid emptying of the viscus, would give an increase of acid from purely physical causes, as already noted.

A large class of patients complaining of gastric indigestion is composed of those in whom the trouble is aggravated or is only present during times of mental stress or worry. Emotional states have a powerful inhibitory action on the processes of digestion. The lack of appetite which accompanies 'love sickness' is proverbial, but ephemeral. It is the more depressing emotions which are of main importance in interfering with digestion, and of these fear and worry are probably responsible for most cases which the general practitioner has to deal with. The following case may be taken as an illustration:-

F.B. Male, aet 62. First complained in October 1920 of discomfort after meals - a feeling of weight in the epigastrium associated with considerable flatulence and some constipation. Had always enjoyed good digestion previously and attributed the present attack to being "rundown" from overwork and business worries. Examination of the abdomen revealed no abnormality. Teeth all artificial and satisfactory. After a few days rest, with attention to the bowels, and a bismuth and bromide mixture, the condition cleared up. Two months later, however, the symptoms recurred, and on being questioned, he again attributed the attack to worry. After this he continued to have digestive troubles at intervals for some two years, at the end of which time he retired from business. His business affairs were satisfactorily settled, but he still continued to suffer from "indigestion". I was confident there was no organic lesion present, but about this time the patient informed me he was afraid he was suffering from cancer of the stomach. In spite of his indigestion he had gradually been gaining in weight, but as this fact did not suffice to reassure him, I sent him to King's College Hospital, where a complete X-ray examination of the abdomen was made; a form of examination in which the patient had complete confidence. The report showed a stomach of normal size and shape, good tone, emptying in five hours, with no evidence of any organic lesion and no abnormality in the intestines. The effect on the patient was magical. In a fortnight he ceased to attend at the Surgery, and for nine months I lost sight of him. In January 1924, however, he reappeared and informed me that his digestion was perfect and he could "eat anything". He had been free of trouble since the X-ray examination.

There can be little doubt that in this case (and similar cases are common enough) the indigestion was of nervous origin, and instituted in the first instance by business worries. Later on the business worries were replaced by the dread of cancer; a state of fear highly favourable to the production of gastrointestinal symptoms. Both of these psychic states, worry and fear, are accompanied by sympathetic stimulation, and it is suggested that the associated indigestion may be due, in part at least, to a concomitant inhibition of the psychic flow of gastric juice, to an interference, that is to say, with the complicated reflex processes which accompany the psychic state of 'appetite'. We have seen, also, that the vagi, in addition to providing the first or psychic portion of gastric juice, also transmit impulses, in the normal animal, which induce a psychic tonus of the gastric muscle, and that this tonus is a necessary factor in normal digestion. It is possible that states of worry and fear, accompanied as they are by activity of the sympathetic, may also cause inhibition of this psychic tonus, and so lead to lessened motility of the stomach as well as diminished secretion. Langdon Brown records the case of a young man who was very nervous during the War at the idea of being called up for military service. X-ray examination showed him to be suffering from atonic dilatation of the stomach. He obtained exemption, and on being re-examined by the X-rays some three months later, showed no sign of gastric atony. Subsequently, when the question of his Military category again came under review, there was a return of the atonic dilatation. Such a condition, as

Langdon Brown says, cannot be simulated. It must be the direct result of a sympathetic inhibition from emotional causes (LANGDON BROWN[146]). The condition is not one of 'atony' so much as active inhibition. As soon as the inhibition is removed, the muscular tone is good.

Worry and fear then, are psychic states which can lead to gastric disorders by causing disturbances of reflexes in an otherwise normal nervous system. Their influence for evil is greatly exaggerated when from any cause the central nervous system is already in a hyper-excitable state. In cases of hysteria, the condition of 'faiblesse irritable' present in the nervous system is commonly reflected in the digestive organs with the production of typical nervous dyspepsia. Poor or depraved appetite, pain after food, flatulence, regurgitation and vomiting are commonly complained of. It some cases the loss of appetite is extreme, and we get an anorexia nervosa in which the patient not only has no desire for food, but feels that she is unable to eat it, and never will be able to eat again. If forced to swallow a few mouthfuls, she probably complains of extreme discomfort, or even of severe pain, and except under compulsion, food is not taken at all.

Under these circumstances, alarming and even fatal emaciation may occur. Osler records a case in which the girl (an adult) weighed only 49 pounds. Postmortem, no lesions were found. Bennett has reported a case in a girl of 16 who showed some disturbance of the normal endocrine balance, and in whom a course of combined thyreoid and pituitary extract had caused diarrhoea and sharp abdominal pain. This experience, coupled to the fact that she was obviously different from other girls, caused her considerable mental anxiety, and she began to complain of severe pain after food, and vomited after every meal. On admission into hospital her weight was just 4 stone; she continued to lose weight, vomited after every meal, and suffered from decided insomnia and abdominal pain. Many careful examinations failed to indicate the presence of any organic disease, and in spite of her assertion that food caused her severe pain, there was no evidence of abdominal tenderness. Explanation to the patient that her fears were greatly exaggerated, and that she could with safety eat full meals apparently convinced her, but did not in the least affect her anorexia. By strong persuasion, however, Bennett was able to induce her to take a full meal, and by remaining with her succeeded also in overcoming her certitude that this would be followed by vomiting. From this time onward she made a steady recovery. In six weeks she was free of all symptoms, and a year later was still perfectly well (BENNETT[147]).

A case such as this illustrates well the effect of abnormal states of the central nervous system in the production of symptoms of gastric disorder. In an extreme case of hysteria the diagnosis is not usually difficult; but in minor degrees, where perhaps the gastric disturbance is the only complaint made by the patient, it is easy to be led astray. It is extremely rare, however, for a hysterical or neurasthenic patient to confine his complaints to one organ or to one system, and in most cases indigestion dependent on a neurasthenic condition of the central nervous system will be accompanied by a list of troubles in other organs, suggestive by its very length. Difficulty is more apt to arise in cases where an organic lesion is complicated by a psychic condition.

The condition of parorexia in which the appetite is preverted and a craving exists for unusual articles of food, or even for unedible and disgusting substances, also depends on a morbid condition of the central nervous system. So also does the opposite condition of sitisphobia, in which there is an undue fastidiousness with regard to certain articles of food, and in which the patient may exclude one article after another until a morbid fear of eating at all is produced. These cases are rare, and call for mental rather than gastric treatment.

It is obvious, however, that states of emotional unbalance play a prominent part in the production of many of the complaints of indigestion met with in general practice. The activities of the autonomic system are not directly under the control of the will, but they respond quickly to emotional states, and to a certain extent, at all events, our emotions can be controlled by our will. The frame of mind in which a meal is eaten has much to do with the ease or difficulty of its subsequent digestion; and this is a fact not sufficiently appreciated by the average patient.

3. Disease of the Sympathetic Ganglia.

It is difficult to say to what extent changes in the sympathetic ganglia may be concerned in the production of disturbed gastrointestinal functions, but it is at least possible that such changes may be responsible for some symptoms of functional gastric disorder. The condition of gastralgia, in which the patient suffers from attacks of very severe pain referred to the epigastrium, sometimes accompanied by vomiting, and usually quite independent of the taking of food have been attributed by some to ganglionic disturbances. So, too, have the somewhat similar pains seen in lead-poisoning, and also the gastric crises of tabes (PURVES STEWART[148]). At present, however, very little has been done in the study of the morbid anatomy of the sympathetic, and until this is altered, many gastric symptoms due to derangement of this system must remain unexplained. There is a wide field here for research which will probably lead to fruitful results in the future.

J. Ch Roux, in France, has devoted some attention to the histological study of the splanchnic nerves in tabes, and states that the lesions of the posterior roots lead to a further degeneration of the preganglionic fibres, passing in these roots to the solar plexus. He believes that the gastric crises of tabes are due to disturbances originated by chronic degenerative changes in the ganglia, and insists also on the occurrence of gastric crises grafted on to a preceding dyspeptic condition, or engendered by a drug-gastritis - particularly potassium iodide.. Ulcer on the lesser curvature, with perigastritis involving the solar plexus is said to be specially efficient in the production of similar attacks of pain and vomiting. If these facts are definitely established, and such conditions as the gastric crises of tabes are proved to be due to ganglionic disturbances, it is at least highly probable that many minor degrees of functional gastric disorder will eventually prove to be due to similar, if less pronounced disorders of the sympathetic ganglia.

In America, Mary Morse has reported a histological study of the sympathetic ganglia in fatal cases of disease. The diseases investigated were of a wide range, and included cases of pellagra, senile dementia, paresis, cerebral syphilis, generalised arteriosclerosis, pernicious anaemia, imbecility and mitral insufficiency, alcoholic dementia and generalised tuberculosis (MARY MORSE[149]).

In no cases were the ganglia normal. Only in the two cases of cerebral syphilis were the the changes found of an insignificant nature, while in all the other cases, well marked or severe lesions, of either diffuse or local distribution, were present. Chronic degenerative changes in the ganglion cells were found in the chronic organic nervous diseases (paresis, senile dementia, cerebral arteriosclerosis). They were also found in ganglia in the vicinity of organs showing chronic lesions. Acute changes (swelling of the nerve cell, fatty degeneration of the sheath) were found in the local ganglia accompanying certain pathological conditions of the organs e.g. valvular heart disease, and acute enteritis and peritonitis. Cases of pellagra, pernicious anaemia and tuberculosis showed both acute and chronic degenerative lesion of the ganglia. The author lays stress on "the special incidence of lesions in the ganglia and their possible correlation with adjacent visceral conditions. In several instances, the lesions were not universally distributed, but were limited to ganglia in the vicinity of affected structures" (MORSE Loc cit. p.25).

These results are very suggestive. Digestive derangement is a common accompaniment to all the diseases included in this investigation, and is constantly present in cases of pellagra. This affection seems to be definitely established now as one of the deficiency diseases, due to a fall of assimilated protein below 40 grammes a day, irrespective of the total caloric value of the diet, and evidence has been adduced that the main effect of this protein deficiency is felt in the sympathetic nervous system. In this connection, the digestive derangements which are a constant feature of pellagra assume particular interest. Epigastric pain and tenderness, flatulence and thirst are always present, and in the later stages, diarrhoea is common. It is possible that these symptoms are directly connected with the lesions observed in the sympathetic ganglia; but at present our knowledge of the morbid anatomy of the sympathetic is too scanty to allow of any dogmatic assertions.

4. Reflected Disturbances.

It is well known that functional disorders of the stomach may occur in association with definite organic disease elsewhere in the alimentary canal, or even outside of it altogether. As Craven Moore says "The gastric functions may be disordered reflexly by a lesion situated more or less remote from the stomach itself. The two essential factors in the production of this condition are the existence of such a lesion, and an increased susceptibility of the reflex nervous mechanism. These may vary indirectly. Thus, some lesions, as a duodenal ulcer, may assert their existence through a nervous mechanism little more susceptible than the normal, while others, as some ileocaecal lesions, may remain latent until the susceptibility becomes greatly exaggerated. There is little doubt that many such cases were formerly classed as nervous dyspepsia. The chief lesions are, duodenal ulcer, cholecystitis, chronic appendicular lesions, ileal kinks, chronic ileocaecal inflammations, caecal and colonic stagnations, diseases of the generative organs in females, motility of the kidneys, diseases of the central nervous system" (MOORE[150]).

In many of these cases, a striking and suggestive feature is the intermittent nature of the gastric symptoms. At times the patient can eat freely and fearlessly an ordinary diet; at other times the ingestion of a biscuit may cause him real suffering. In some of these cases the dyspeptic symptoms are undoubtedly associated with variations in the peristaltic movements, which may be temporarily increased or decreased; in others with alterations in the secretory activities of the glands, and sometimes, no doubt, a combination of both factors is present. Hyperchlorhydria is a common result of organic disease of the alimentary tract. It may occur from lesions in the stomach itself. It is frequently present in lesions of the appendix, in duodenal ulcer, in gall stones. It occurs also in pancreatitis, in chronic inflammation of the intestine, in pulmonary tuberculosis, and as a result of eyestrain (POTTENGER[151]). Langdon Brown believes that in many cases of reflex hyperchlorhydria, the increase of acid is due to spasm of the pylorus preventing the escape of acid into the duodenum, and he regards this as a protective mechanism. In support of this contention he quotes Murphy and Cannon's experiment in which they found that after high intestinal section and suture, the pylorus remained tightly closed for about six hours after recovery from the anaesthesia; a period of time sufficient for the primary cementing of the intestinal wound (CANNON and MURPHY[152]). "This is clearly protective, and helps to explain the spasm and the consequent hyperchlorhydria of reflex dyspepsia. It is a pathological extension of Elliott's law of the hollow viscus. Thus we see that the same condition which inhibits movements in the affected segments leads to spasm of the associated sphincter" (LANGDON BROWN[153]).

This is an interesting conception which probably accounts for the hyperchlorhydria seen in some cases of reflex dyspepsia; but the purposive protective element cannot apply to cases in which the increase of acid is due to a moveable kidney or to a retroverted uterus, examples of which are commonly enough met with.

The following case illustrates the type of dyspepsia met with in cases of chronic appendicular lesions.

L.W. aet 36., Male. Complains of pain in the epigastrium several hours after food, with heart-burn, and flatulence. Temporary relief follows the taking of more food. Patient attributes his troubles to poor food in the Army, as previous to joining the Forces he had never had any digestive discomfort except a tendency to constipation. On three occasions during the past year he has had attacks of "acute indigestion" with vomiting and severe pain, each attack lasting for several days, but between the attacks has had periods when his digestion caused him no trouble at all. The report of X-ray examination after a bismuth meal was as follows:-

Immediately after -

Stomach of steerhorn type, normal in position, tone and outline. Duodenal cap not visible.

Two hours after -

Stomach emptying rapidly, appears to be normal in outline. Duodenal cap visible, not very well filled, but appears regular in outline.

Five hours after -

Considerable residue in stomach. Duodenal cap is not well filled, outline is not quite regular. Head of the meal is entering the transverse colon.

Eight hours after -

The stomach is empty. The head of the meal has made no progress. The caecum remains well filled.

Twenty-four hours after -

The caecum remains well filled, as also do the ascending colon, and the transverse colon. There is visible an imperfectly filled appendix.

Forty-eight hours after -

(Bowels have acted). Considerable residue from hepatic to splenic flexure. Appendix well seen.

In this case no test meal was given. The clinical history, however, and the X-ray appearances pointed to spasm of the pylorus, due to an extrinsic reflex, the origin of the reflex being probably a diseased appendix. At operation a chronically inflamed appendix was found, and removed, with complete recovery and disappearance of all symptoms.

In such cases of reflex dyspepsia, the test meal may show hyperchlorhydria, but it frequently does not. Langdon Brown explains this discrepancy between the symptoms and the test meal on the hypothesis that the excess of acid in these cases is due simply to pyloric spasm and not to over-secretion (LANGDON BROWN[154]). The test meal is usually withdrawn at the end of the first hour, at which time the spasm has not come on, and hence the excess of acid is not present. Diverticulitis produces hyperchlorhydria in the same way and of the same type, as appendicitis. "The general conclusion as to hyperchlorhydria, then, is that it is usually due to some reflex cause - an irritable focus somewhere lower down in the alimentary canal, and that the high acidity of the test meal does not mean oversecretion, but retention of the gastric contents due to pyloric spasm. The more excitable the nervous system, the lower is the threshold stimulus required to initiate symptoms. Inhibition of segments of the alimentary canal, and stimulation of the sphincters, both due to the sympathetic, play a large part in the production of this type (LANGDON BROWN[155]).

The occurrence of hyperchlorhydria from overaction of the secretory fibres of the vagus has already been noted. Excess of acid is often present, even though no symptoms are complained of, in strong and young subjects with good appetites, Emotional disturbances may sometimes cause a diminution in HCL, but they may also cause an increase of acidity; hyperchlorhydria is a common feature of emotional disturbances, grief, worry, overwork, and hysteria (MACLENNAN[156]).

In place of hyperchlorhydria and its associated spasm, it is possible that an irritative focus in the alimentary canal, by stimulating the sympathetic, may cause an actual inhibition of the gastric musculature, with a consequent gastric atony. As an illustration of this, Langdon Brown quotes the following case (LANGDON BROWN[157]):-

The patient, a male, aged about 30, gave a history of pain and flatulence half an hour after food, for the preceding twelve months. Latterly the pain did not occur till four or five hours after food. A well-marked succussion splash could be obtained, and X-ray examination showed great dilatation and atony, and the greater curvature extended as low as the pubes. Nevertheless the test meal gave a total acidity of 0.29 per cent, the physiologically active hydrochloric acid being as high as 0.27 per cent. Lavage of the stomach caused marked improvement. Some two years later he was admitted to hospital suffering from an acute abdominal attack, and at the operation (performed under the impression that the stomach was the offending viscus), a gangrenous appendix was found and removed. Examination subsequently showed that the dilatation of the stomach had completely disappeared, and the test meal gave a normal reading of 0.195 per cent of acidity.

In this case, the diseased appendix seems to have been responsible both for hyperchlorhydria and for atonic dilatation of the stomach, and Brown concludes that when atonic dilatation is combined with hyperchlorhydria, an irritative focus causing reflex dyspepsia and sympathetic inhibition should be looked for.

It thus appears that disease elsewhere in the alimentary canal may give rise to hyper-chlorhydria and pain in the stomach, from reflex spasm of the pylorus and increased tone and peristalsis of the gastric musculature. The normal harmonious relations between the peristaltic activities of the stomach wall and the opening and closing of the pylorus are interfered with, and as a result symptoms are produced indicative of derangements of the functions of this organ. In other instances, the irritative focus leads to the opposite condition of loss of tone in the gastric muscles, produced again by abnormal or exaggerated reflex processes through the sympathetic nerves. Even in the latter case, reflex spasm of the pylorus may also be present, in which case pain and hyperchlorhydria will be associated with the loss of muscular tone.

<u>CONCLUSIONS.</u>

1. Many symptoms of disease, as pointed out by Mackenzie, are produced by disturbances of normal reflex processes occurring in the body.

2. Such disturbances may occur at any point in the reflex arc, and may lead to increased activity of the end organ, or diminished activity, or to a change of the end result altogether (reversal of reflexes); or to interference with other reflexes co-ordinating the activities of different organs, or different parts of the same organ.

3. Our knowledge of the reflex processes occurring normally in the gastrointestinal canal is incomplete, and hence our knowledge of those occurring under abnormal conditions is also unsatisfactory.

4. One factor in this lack of knowledge, is absence of precise information concerning the afferent side of the autonomic system.

5. A second factor of equal importance is lack of knowledge of the effects produced by diseased conditions of the sympathetic ganglia; and a study of the effects on the functions of

the gastrointestinal tract of irritative and paralysing lesions of these ganglia would probably lead to valuable results.

6. In the case of functional disorders of the stomach, disturbances of normal reflexes, leading to symptoms, may arise from:-

1. Abnormal state of the nerves.
2. Abnormal state of the central nervous system.
3. Abnormal state of the sympathetic ganglia.
4. Diseased conditions elsewhere in the alimentary tract or even outside it.

7. Further information is desirable as to the exact functions of the plexuses of Meissner and of Auerbach; as to the exact relationship between these plexuses and the sympathetic nerves; and as to the manner in which the activities of these local nervous mechanisms are influenced by impulses from the extrinsic nerves.

8. In particular, the question of the tonus of the gastric musculature, and the part played in its regulation under normal and abnormal conditions, by the local nerve mechanisms and the extrinsic nerves respectively, requires further elucidation.

9. A study of the symptoms in cases of functional gastric disorder is of fundamental importance. Exact knowledge of the particular reflexes that are disturbed, and of the manner in which the disturbance is produced, will lead to the discovery of the underlying cause, the removal of which is the main object of treatment.

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